Compounds for the inhibition of rotamases

The present invention is related to new compounds and the use of said compounds as an inhibitor to rotamases, for the manufacture of medicaments, for removing a rotamase from a sample, for identifying a rotamase in a sample, for the manufacture of an affinity device, in drug potentiation applications and methods of treating a patient.

Rotamases, also referred to as peptidyl-prolyl *cis*-trans isomerases (PPIases) are a class of enzymes important in protein folding, assembly and transport. They act as catalysts to promote isomerization about the peptidyl-prolyl bond, which can have profound effects on protein function.

PPIases are divided into three families, cyclophilins, FK-506 binding proteins (FKBPs) and the Pin1/parvulin family. While cyclophilins and FKBPs are distinguished by their ability to bind immunosuppressant molecules cyclosporin and FK-506, respectively, the Pin1/parvulin family binds neither of these immunosuppressants and is structurally unrelated to the other two families. Known members of the Pin1/parvulin class include Pins 1 – 3 (Lu et al., Nature 380:544-547, 1996), Pin-L (Campbell et al., Genomics 44:157-162, 1997), parvulin (Rahfeld et al., FEBS Letts 352:180-184, 1994), dodo (Maleszka et al., Proc Natl Acad Sci USA 93:447-451, 1996) and Ess1/Pft1 (Hanes et al., Yeast 5:55-72, 1989; and Hani et al., FEBS Letts 365:198-202, 1995).

Recent research suggests that members of the Pin1/parvulin family are essential modulators of the cell cycle, and mitosis in particular. Lu et al., Nature 380:544-547, 1996 reports that depletion of Pin1/Ess1 in yeast or human cells induces mitotic arrest followed by apoptosis, indicating that enzymes in this family serve an essential function in cell division and proliferation.

Accordingly, compounds inhibiting rotamases can serve as agents for the treatment of a variety of disorders which are characterized by an inappropriate cell proliferation including cancer and infectious diseases.

In the prior art a huge number of compounds are described which are active as inhibitors to rotamase. The respective compounds are, among others, peptide derivatives such as amino

methylene-peptides which are described in European patent EP 0 610 743, or non-peptidic or non-peptidomimetic molecules.

Given the importance of rotamase there is an ongoing need in the art to provide further compounds which are suitable as inhibitors to rotamases and thus suitable to be used as a medicament for those diseases wherein a rotamase is involved in the pathological mechanism.

Accordingly, the problem underlying the present invention is to provide compounds which inhibit a rotamase. A further problem underlying the present invention is to provide new compounds for the treatment of diseases the pathophysiology of which involves an imbalanced or undesired activity of a rotamase. A still further problem underlying the present invention is to provide means for the isolation and/or identification of rotamases.

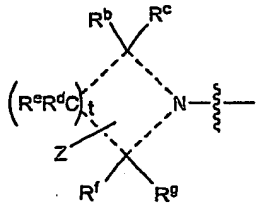
In a first aspect the problem underlying the present invention is solved by a compound of formula (I):

A-B-E-D (I)

wherein:

A is selected from the group comprising

R^a-L1-K-L2-,

and 

wherein the dashed lines indicate each and independently a single or a double bond;

wherein K is selected from the group comprising

C=T,

O, S, S(O) and $S(O_2)$,

or is absent,

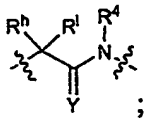
with =T being selected from the group comprising

= O, =S, =N–R^1, =N–CN, =N–NO_2 and =CH–NO_2,

L1 and L2 are each and independently selected from the group comprising O, S and amines, preferably NR^2, NR^3;

or being individually and independent from each other absent;

B is either present or absent, but if B is present then B is



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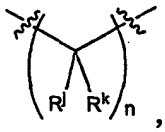
E is  ,

whereby n is any integers from 1 to 5

whereby if n is 2 or more, any of the group(s) –(CR^jR^k)– which are present, can be the same as or different from any other of the group(s) –(CR^jR^k)–,

whereby any group –(CR^jR^k)– is linked to any other group –(CR^jR^k)– or any moiety of the compound through a bond, whereby the bond is selected from the group comprising single bonds, double bonds and triple bonds;

D is selected from the group comprising –(CR^lR^m)$_r$C(O)H, -(CR^lR^m)$_r$C≡N, –(CR^lR^m)$_r$NHNHC(O)NR^5R^6, –(CR^lR^m)$_r$C(O)(CR^nR^o)$_r$C(O)OR^7, –(CR^lR^m)$_r$C(O)(CR^nR^o)$_r$C(O)NR^8R^9, –(CR^lR^m)$_r$CH(OH)(CR^nR^o)$_r$C(O)U, -(CR^lR^m)$_r$C(O)W –(CR^lR^m)$_r$C(O)CH_2W, –(CR^lR^m)$_r$C(O)haloalkyl, and -(CR^lR^m)$_r$C(O)(CR^nR^o)$_r$$CHN_2$,

whereby

U is –OR^{10} or –$NR^{11}R^{12}$, and

W is $-OR^{13}$, $-SR^{14}$, $-NR^{15}R^{16}$, or a heterocyclic moiety,

whereby r and r′ are any integers from 0 to 5 and any r and r′mentioned are independently selected from any other r and r′ mentioned or present,

whereby if r is 2 or more, any of the group(s) $-(CR^lR^m)-$ which are present, can be the same as or different from any of the other group(s) $-(CR^lR^m)-$,

whereby any group $-(CR^lR^m)-$ is linked to any other group $-(CR^lR^m)-$ or any moiety of the compound through a bond, whereby the bond is selected from the group comprising single bonds, double bonds and triple bonds,

whereby if r′ is 2 or more, any of the group(s) $-(CR^nR^o)-$ which are present, can be the same as or different from any of the other group(s) $-(CR^nR^o)-$,

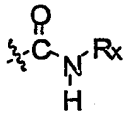
whereby any group $-(CR^nR^o)-$ is linked to any other group $-(CR^nR^o)-$ or any moiety of the compound through a bond, whereby the bond is selected from the group comprising single bonds, double bonds and triple bonds;

Y is selected from the group comprising O, S, N-CN, $N-NO_2$, $CH-NO_2$ or NR^{17}, wherein R^{17} is selected from the group comprising H, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylcycloalkyl, substituted alkylcycloalkyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl, heterocyclyl, substituted heterocyclyl, alkylheterocyclyl, substituted alkylheterocyclyl, heteroaryl, substituted heteroaryl, alkylheteroaryl and substituted alkylheteroaryl;

t is any integer from 1 to 6,

whereby if t is 2 or more, any of the group(s) $-(CR^dR^e)-$ which are present, can be the same as or different from any of the other group(s) $-(CR^dR^e)-$,

whereby any group $-(CR^dR^e)-$ is linked to any other group $-(CR^dR^e)-$ or any moiety of the compound through a bond, whereby the bond is selected from the group comprising single bonds, double bonds and triple bonds;

Z is 

, whereby R_X is selected from the group comprising amino acids, peptides, alkyl, substituted alkyl, straight alkyl, substituted straight alkyl, branched alkyl, substituted branched alkyl; or is absent; and Z is attached to any of the carbon of the cyclic structure;

R^a, R^b, R^c, R^d, R^e, R^f, R^g, R^h, R^i, R^j, R^k, R^l, R^m, R^n and R^o are each and independently from each other selected from the group comprising H, OR^{18}, SR^{19}, $NR^{20}R^{21}$, halo, alkyl, substituted alkyl, straight alkyl, substituted straight alkyl, branched alkyl, substituted branched alkyl, straight alkenyl, substituted straight alkenyl, branched alkenyl , substituted branched alkenyl, straight alkynyl, substituted straight alkynyl, branched alkynyl, substituted branched alkynyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclyl, substituted heterocyclyl, mono-unsaturated heterocyclyl, poly-unsaturated heterocyclyl, mono-substituted poly-unsaturated heterocyclyl, poly-substituted poly-unsaturated heterocyclyl, mono-substituted mono-unsaturated heterocyclyl, poly-substituted mono-unsaturated heterocyclyl, aryl, substituted aryl, heteroaryl and substituted heteroaryl; or may be independently from each other absent;

wherein, optionally, R^d and R^f, R^d and R^b, R^d and R^c are linked so as to form a ring saturated or unsaturated comprising 4 to 12 members, preferably 5 to 10 members;

wherein R^1, R^2, R^3 and R^4 are selected from the group comprising H, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylcycloalkyl, substituted alkylcycloalkyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl, heterocyclyl, substituted heterocyclyl, alkylheterocyclyl, substituted alkylheterocyclyl, heteroaryl, substituted heteroaryl, alkylheteroaryl and substituted alkylheteroaryl; and

R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{18}, R^{19}, R^{20} and R^{21} are each and independently selected from the group comprising H, alkyl, substituted alkyl, aryl, substituted aryl, alkylaryl, substituted alkylaryl, alkoxy, substituted alkoxy, aryloxy, substituted aryloxy, alkylamino, substituted alkylamino, arylamino and substituted arylamino;

or is a pharmaceutically acceptable salt, solvate, hydrate or prodrug thereof.

As used herein in preferred embodiment "$\sim\!\!\sim$" denotes any linkage to any other radical, moiety group or component of a compound, preferably of any compound as disclosed or described herein.

In an embodiment R^b, R^c, R^d, R^e, R^f and R^g are each and independently from each other selected from the group comprising H and alkyl, preferably lower alkyl.

In an embodiment the dashed lines indicate a single bond.

In an embodiment K is selected from the group comprising

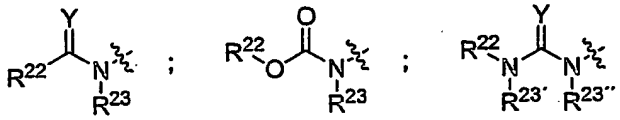
C = T
SO, $S(O_2)$
with = T being = O or = S.

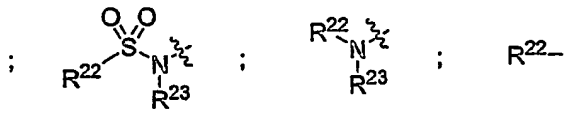
In an embodiment L1 and L2 are each and independently selected from the group comprising NR^2 and NR^3.

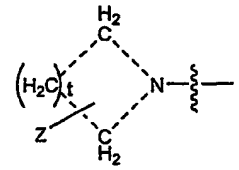
In a preferred embodiment R^2 and R^3 are each and independently selected from the group comprising H and alkyl, preferably lower alkyl.

In an embodiment

A is selected from the group comprising





and 

R^{22} is selected from the group comprising H, halogen, alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl and derivatives of any of these groups; and

R^{23}, $R^{23'}$, $R^{23''}$ are each independently selected from the group consisting of H, alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl and derivatives of any of these groups or is a pharmaceutically acceptable salt or prodrug thereof.

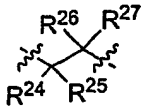
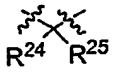
In an embodiment Y is selected from the group comprising O, S and NR^{17}, more preferably selected from the group comprising O and S.

In an embodiment, preferably an embodiment of the preceeding embodiment R^4 is selected from the group comprising H and alkyl.

In a preferred embodiment the alkyl is a lower alkyl, preferably methyl.

In an embodiment n is 1 or 2.

In an embodiment, preferably an embodiment of the preceeding embodiment

E is  or 

and

R^{24}, R^{25}, R^{26}, and R^{27} are each individually and independently selected from the group comprising H, halogen, alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl and derivatives of any of these groups.

In an embodiment, preferably any of the two preceeding embodiments, if n = 1, then r is different from 0.

In an alternative embodiment, if n = 2, then r is any integer from 0 to 5, preferably 0, 1 or 2.

In an embodiment

D is selected from the group comprising $-(CH_2)_rC(O)H$, $-(CH_2)_rC\equiv N$, $-(CH_2)_rNHNHC(O)NR^5R^6$, $-(CH_2)_rC(O)(CH_2)_r-C(O)OR^7$,

$-(CH_2)_r C(O)(CH_2)_{r'} C(O)NR^8R^9$, $-(CH_2)_r CH(OH)(CH_2)_{r'} C(O)U$, $-(CH_2)_r C(O)W$ $-(CH_2)_r C(O)CH_2W$, $-(CH_2)_r C(O)$haloalkyl, and $-(CH_2)_r C(O)(CH_2)_{r'} CHN_2$;

whereby

U is $-OR^{10}$ or $-NR^{11}R^{12}$; and

W is $-OR^{13}$, $-SR^{14}$, $-NR^{15}R^{16}$, or a heterocyclic moiety;

whereby r and r′ is are any integers from 0 to 5 and any r and r′mentioned are independently selected from any other r and r′ mentioned or present and whereby any of R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, R^{15}, and R^{16} are each and independently selected from the group comprising H, alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl and derivatives of any of these groups.

In an embodiment D is $-(CR^lR^m)_r C\equiv N$.

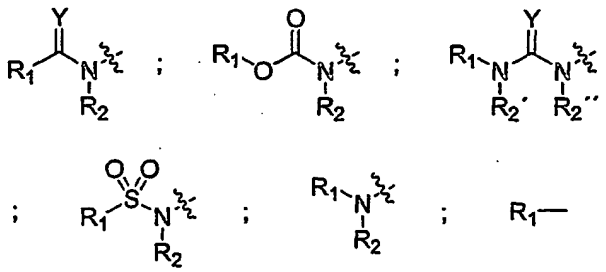
In an embodiment t is 2, 3 or 4.

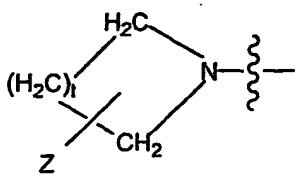
In a second aspect of the present invention which is preferably an embodiment of the first aspect of the present invention the problem underlying the present invention is solved by a compound having the structure of formula (I)

A-B-E-D (I)

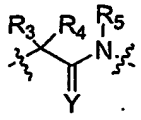
wherein:

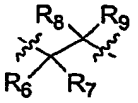
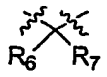
A is selected from the group comprising



and 

B is either present or absent, but if B is present, B is



E is  or 

D is selected from the group comprising $-(CH_2)_rC(O)H$, $-(CH_2)_rC \equiv N$, $-(CH_2)_rNHNHC(O)NR_{A'}R_{A''}$, $-C(CH_2)_rC(O)(CH_2)_rC(O)OR_{A'}$, $-(CH_2)_rC(O)(CH_2)_rC(O)NR_{A'}R_{A''}$, $-(CH_2)_rCH(OH)(CH_2)_rC(O)U$, $-(CH_2)_rC(O)W$ $-(CH_2)_rC(O)CH_2W$, $-(CH_2)_rC(O)$haloalkyl, and $-(CH_2)_rC(O)(CH_2)_rCHN_2$;

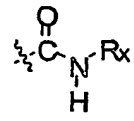
whereby U is $-OR_{A'}$ or $-NR_{A'}R_{A''}$; and

W is $-OR_{A'}$, $-SR_{A'}$, $-NR_{A'}R_{A''}$, or a heterocyclic moiety;

whereby r and r′ are any integer from 0 to 5 and any r and r′mentioned are independently selected from any other r and r′mentioned or present; and whereby $R_{A'}$ and $R_{A''}$ are selected independently from the group comprising H, alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl and derivatives of any of these groups;

Y is O, S, or NR_a wherein R_a is selected from the group comprising H, alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl and derivatives of any of these groups;

t is 1, 2 or 3;

Z is 

, whereby R_X is selected from the group comprising amino acids, peptides and alkyl;

R_1, R_3, R_4, R_6, R_7, R_8, and R_9 are each individually and independently selected from the group comprising H, halogen, alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl and derivatives of any of these groups;

R_2, R_2', R_2'', R_5 are each independently selected from the group consisting of H, alkyl, cycloalkyl, aryl, heteroaryl and heterocyclyl and derivatives of any of these groups or is a pharmaceutically acceptable salt or prodrug thereof; and

whereby "〰" denotes any linkage to A, B, E and D, respectively.

In a preferred embodiment each of R_1, R_3, R_4, R_6, R_7, R_8 and R_9 is individually and independently a derivative of any of alkyl, cycloalkyl, aryl, heterocyclyl, or heteroaryl,

whereby any of these groups is individually and independently substituted by one or more groups of the formula R_b,

> whereby R_b is selected from the group comprising alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkoxy, aryloxy, arylalkoxy, alkoxycarbonyl, aryloxycarbonyl, alkanoyl, aroyl, alkanoyloxy, aroyloxy, carbamoyl, carbamoyl derivative, alkanoylamino, aroylamino, alkylthio, alkylthio derivatives, arylthio, arylthio derivatives, ureido, ureido derivatives, alkoxycarbonylamino, aryloxycarbonylamino, alkylcarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl, amino, amino derivatives

and preferably R_b is further substituted by one or more R_c,

> whereby R_c is selected from the group comprising alkyl, cycloalkyl, aryl, arylalkyl, alkoxy, aryloxy, arylalkoxy, alkanoyl, aroyl, amino, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino.

In a further embodiment of the inventive compounds the carbamoyl group is derivatized, preferably the nitrogen atom is independently mono- or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl; and/or

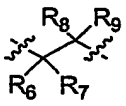
the alkylthio group is derivatized, preferably the sulfur atom is oxidized to a sulfoxide or sulfone; and/or

the arylthio group is derivatized, preferably the sulfur atom is oxidized to a sulfoxide or sulfone; and/or

the ureido group is derivatized, preferably either the nitrogen atom is independently mono- or di-substituted by a group which is selected from the group comprising alkyl, aryl, heterocyclyl or heteroaryl, alkoxycarbonylamino, aryloxycarbonylamino, alklycarbamoyloxy, arylcarbamoyloxy, alkylsulfonylamino, arylsulfonylamino, alkylaminosulfonyl, arylaminosulfonyl; and/or

the amino group is derivatized, preferably the nitrogen atom is independently mono- or di-substituted by alkyl, aryl, heterocyclyl or heteroaryl, halogen, hydroxy, oxo, carboxy, cyano, nitro, amidino and guanidino.

In a particularly preferred embodiment B is present and has the meaning as defined in any of the preceding claims,

E is 

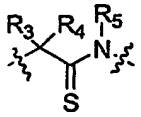
with R_6 to R_9 having the meaning as defined in any aspect or embodiment as specified herein.

In a more preferred embodiment D is selected from the group comprising $-(CH_2)_r C(O)H$, $-(CH_2)_r C \equiv N$, $-(CH_2)_r NHNHC(O)NR_{A'}R_{A''}$, $-C(CH_2)_r C(O)(CH_2)_r C(O)OR_{A'}$, $-(CH_2)_r C(O)(CH_2)_r C(O)NR_{A'}R_{A''}$, $-(CH_2)_r CH(OH)(CH_2)_r C(O)U$, $-(CH_2)_r C(O)W$,

whereby U is $-OR_{A'}$ or $-NR_{A'}R_{A''}$; W is $-OR_{A'}$, $-SR_{A'}$, $-NR_{A'}R_{A''}$, or a heterocyclic moiety; r and r' are independently any integer from 0 to 5; and $R_{A'}$ and $R_{A''}$ are selected independently from the group comprising H, alkyl, phenyl, benzyl, and phenethyl.

In an even more preferred embodiment D is $-(CH_2)_r C \equiv N$ and r is any integer from 0 to 3.

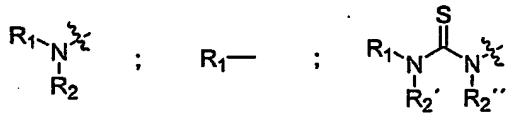
In a further preferred embodiment

B is 

In a particularly preferred embodiment using the substituent B as defined above, D is selected from the group comprising $-(CH_2)_rC(O)H$, $-(CH_2)_rC \equiv N$, $-(CH_2)_rNHNHC(O)NR_{A'}R_{A''}$, $-C(CH_2)_rC(O)(CH_2)_rC(O)OR_{A'}$, $-(CH_2)_rC(O)(CH_2)_rC(O)NR_{A'}R_{A''}$, $-(CH_2)_rCH(OH)(CH_2)_rC(O)U$, $-(CH_2)_rC(O)W$, whereby U is $-OR_{A'}$ or $-NR_{A'}R_{A''}$, W is $-OR_{A'}$, $-SR_{A'}$, $-NR_{A'}R_{A''}$, or a heterocyclic moiety; r and r′ are independently any integer from 0 to 5; and $R_{A'}$ and $R_{A''}$ are selected independently from the group comprising H, alkyl, phenyl, benzyl, and phenethyl.

In an even more preferred embodiment D is $-(CH_2)_rC \equiv N$ and r is any integer from 0 to 3.

In a further embodiment of the compounds according to the present invention

A is  ; ;

or a pharmaceutically acceptable salt or prodrug thereof.

In a preferred embodiment of the inventive compounds having A substituted as described above, D is selected from the group comprising $-(CH_2)_rC(O)H$, $-(CH_2)_rC \equiv N$, $-(CH_2)_rNHNHC(O)NR_{A'}R_{A''}$, $-C(CH_2)_rC(O)(CH_2)_rC(O)OR_{A'}$, $-(CH_2)_rC(O)(CH_2)_rC(O)NR_{A'}R_{A''}$, $-(CH_2)_rCH(OH)(CH_2)_rC(O)U$, $-(CH_2)_rC(O)W$; whereby U is $-OR_{A'}$ or $-NR_{A'}R_{A''}$, W is $-OR_{A'}$, $-SR_{A'}$, $-NR_{A'}R_{A''}$, or a heterocyclic moiety; $R_{A'}$ and $R_{A''}$ are independently selected from H, alkyl, phenyl, benzyl, and phenethyl; and r and r′ are independently any integer from 0 to 5. In an even more preferred embodiment D is $-(CH_2)_rC \equiv N$ and r is any integer from 0 to 3.

In a further embodiment of the compounds according to the present invention B is absent and the other residues have the same meaning as discussed in any of the aforementioned aspects and embodiments, respectively, of the present invention.

In an even preferred embodiment with B being absent, D is selected from the group comprising $-(CH_2)_rC(O)H$, $-(CH_2)_rC\equiv N$, $-(CH_2)_rNHNHC(O)NR_{A'}R_{A''}$, $-C(CH_2)_rC(O)(CH_2)_rC(O)OR_{A'}$, $-(CH_2)_rC(O)(CH_2)_rC(O)NR_{A'}R_{A''}$, $-(CH_2)_rCH(OH)(CH_2)_rC(O)U$, $-(CH_2)_rC(O)W$;

whereby U is $-OR_{A'}$ or $-NR_{A'}R_{A''}$, W is $-OR_{A'}$, $-SR_{A'}$, $-NR_{A'}R_{A''}$, or a heterocyclic moiety; $R_{A'}$ and $R_{A''}$ are independently selected from H, alkyl, phenyl, benzyl, and phenethyl; and r and r' are independently any integer from 0 to 5. In a more preferred embodiment D is $-(CH_2)_rC\equiv N$ and r is any integer from 0 to 3.

Particularly preferred compounds according to the present invention are the compounds specified in the following table:

3-(1*H*-Indol-3-yl)-2-acetylamino-propionic acid cyanomethyl-amide,
3-(1*H*-Indol-3-yl)-2-[3-(4-trifluoromethyl-phenyl)-ureido]-propionic acid cyanomethyl-amide,
3-(1*H*-Indol-3-yl)-2-[3-(4-trifluoromethylsulfanyl-phenyl)-ureido]-propionic acid cyanomethyl-amide,
3-(1*H*-Indol-3-yl)-2-[3-(4-trifluoromethoxy-phenyl)-ureido]-propionic acid cyanomethyl-amide,
3-(1*H*-Indol-3-yl)-2-[3-(4-cyano-phenyl)-ureido]-propionic acid cyanomethyl-amide,
3-(1*H*-Indol-3-yl)-2-(3-benzyl-ureido)-propionic acid cyanomethyl-amide,
3-(1*H*-Indol-3-yl)-2-(3-*o*-tolyl-ureido)-propionic acid cyanomethyl-amide,
3-(1*H*-Indol-3-yl)-2-[3-(*S*)-(1-phenyl-ethyl)-ureido]-propionic acid cyanomethyl-amide,
3-(1*H*-Indol-3-yl)-2-[3-(2,6-dimethyl-phenyl)-ureido]-propionic acid cyanomethyl-amide,
3-(1*H*-Indol-3-yl)-2-[3-(3-methyl-benzyl)-ureido]-propionic acid cyanomethyl-amide,
3-(1*H*-Indol-3-yl)-2-[3-(1,1,3,3-tetramethyl-butyl)-ureido]-propionic acid cyanomethyl-amide,
3-(1*H*-Indol-3-yl)-2-(3-indan-5-yl-ureido)-propionic acid cyanomethyl-amide,
3-(1*H*-Indol-3-yl)-2-[3-(2-phenyl-cyclopropyl)-ureido]-propionic acid cyanomethyl-amide,
3-(1*H*-Indol-3-yl)-2-(3-adamantan-1-yl-ureido)-propionic acid cyanomethyl-amide,
3-(1*H*-Indol-3-yl)-2-(3-biphenyl-4-yl-ureido)-propionic acid cyanomethyl-amide,
3-(1*H*-Indol-3-yl)-2-[3-(4-phenoxy-phenyl)-ureido]-propionic acid cyanomethyl-amide,
3-(1*H*-Indol-3-yl)-2-[3-(4-nitro-phenyl)-ureido]-propionic acid cyanomethyl-amide,
3-(1*H*-Indol-3-yl)-2-(3-cyclohexyl-ureido)-propionic acid cyanomethyl-amide,
3-(1*H*-Indol-3-yl)-2-(3-benzo[1,3]dioxol-5-yl-ureido)-propionic acid cyanomethyl-amide,
3-(1*H*-Indol-3-yl)-2-[3-(2-fluoro-benzyl)-ureido]-propionic acid cyanomethyl-amide,
3-(1*H*-Indol-3-yl)-2-[3-(4-methyl-benzyl)-ureido]-propionic acid cyanomethyl-amide,

3-(1*H*-Indol-3-yl)-2-(3-phenethyl-ureido) -ureido]-propionic acid cyanomethyl-amide,

3-(1*H*-Indol-3-yl)-2-[3-(3,4,5-trimethoxy-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-(1*H*-Indol-3-yl)-2-(3-ethyl-thioureido)-propionic acid cyanomethyl-amide,

3-(1*H*-Indol-3-yl)-2-(3-isopropyl-thioureido)-propionic acid cyanomethyl-amide,

3-(1*H*-Indol-3-yl)-2-[3-(4-nitro-phenyl)-thioureido]-propionic acid cyanomethyl-amide,

3-(1*H*-Indol-3-yl)-2-(3-phenyl-thioureido)-propionic acid cyanomethyl-amide,

3-(1*H*-Indol-3-yl)-2-[3-(4-trifluoromethoxy-phenyl)-thioureido]-propionic acid cyanomethyl-amide,

3-(1*H*-Indol-3-yl)-2-{3-[4-(2,2,2-trifluoro-ethyl)-phenyl]-thioureido}-propionic acid cyanomethyl-amide,

3-(1*H*-Indol-3-yl)-2-[3-(4-methoxy-phenyl)-thioureido]-propionic acid cyanomethyl-amide,

3-(1*H*-Indol-3-yl)-2-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-ylmethanesulfonylamino)-propionic acid cyanomethyl-amide,

3-(1*H*-Indol-3-yl)-2-(thiophene-2-sulfonylamino)-propionic acid cyanomethyl-amide,

3-(1*H*-Indol-3-yl)-2-(4-trifluoromethoxy-benzenesulfonylamino)-propionic acid cyanomethyl-amide,

3-(1*H*-Indol-3-yl)-2-(4-*tert*-butyl-benzenesulfonylamino)-propionic acid cyanomethyl-amide,

3-(1*H*-Indol-3-yl)-2-(4-chloro-benzenesulfonylamino)-propionic acid cyanomethyl-amide,

3-(1*H*-Indol-3-yl)-2-(4-methoxy-benzenesulfonylamino)-propionic acid cyanomethyl-amide,

3-(1*H*-Indol-3-yl)-2-(quinoline-6-sulfonylamino)-propionic acid cyanomethyl-amide,

3-(1*H*-Indol-3-yl)-2-benzenesulfonylamino-propionic acid cyanomethyl-amide,

1-Methyl-1*H*-indole-2-carboxylic acid [1-(cyanomethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-amide,

2-Propyl-pentanoic acid [1-(cyanomethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-amide,

1-Methyl-cyclopropanecarboxylic acid [1-(cyanomethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-amide,

Thiophene-2-carboxylic acid [1-(cyanomethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-amide,

N-[1-(Cyanomethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-3-trifluoromethyl-benzamide,

Biphenyl-2-carboxylic acid [1-(cyanomethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-amide,

4-Acetylamino-*N*-[1-(cyanomethyl-carbamoyl)-2-(1H-indol-3-yl)-ethyl]-benzamide,

3-(1*H*-Indol-3-yl)-2-(2-1*H*-indol-3-yl-acetylamino)-propionic acid cyanomethyl-amide,

3-(1*H*-Indol-3-yl)-2-(3-1*H*-indol-3-yl-propionylamino)-propionic acid cyanomethyl-amide,

N-[1-(Cyanomethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-4-(1*H*-indol-3-yl)-butyramide,

N-[1-(Cyanomethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-benzamide,

3-Chloromethyl-*N*-[1-(cyanomethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-benzamide,

4-Chloromethyl-*N*-[1-(cyanomethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-benzamide,

N-[1-(Cyanomethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-2-fluoro-benzamide,

N-[1-(Cyanomethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-2-nitro-benzamide,

N-[1-(Cyanomethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-acrylamide,

3-(1*H*-Indol-3-yl)-2,2-dimethyl-propionic acid cyanomethyl-amide,

3-(1*H*-Indol-3-yl)-2-(2-methoxy-acetylamino)-propionic acid cyanomethyl-amide,

N-[1-(Cyanomethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-oxalamic acid methyl ester,

N-[1-(Cyanomethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-phthalamic acid,

N-[1-(Cyanomethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-succinamic acid,

3-[1-(Cyanomethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethylcarbamoyl]-acrylic acid,

[1-(Cyanomethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-carbamic acid isobutyl ester,

[1-(Cyanomethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-carbamic acid butyl ester,

[1-(Cyanomethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-carbamic acid hexyl ester,

[1-(Cyanomethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-carbamic acid *tert*-butyl ester,

[1-(Cyanomethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-carbamic acid methyl ester,

[1-(Cyanomethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-carbamic acid ethyl ester,

[1-(Cyanomethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-carbamic acid 9*H*-fluoren-9-ylmethyl ester,

3-(1*H*-Indol-3-yl)-2-acetylamino-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-[3-(4-trifluoromethyl-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-[3-(4-trifluoromethylsulfanyl-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-[3-(4-trifluoromethoxy-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-[3-(4-cyano-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-(3-benzyl-ureido)-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-(3-o-tolyl-ureido)-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-[3-(*S*)-(1-phenyl-ethyl)-ureido]-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-[3-(2,6-dimethyl-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-[3-(3-methyl-benzyl)-ureido]-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-[3-(1,1,3,3-tetramethyl-butyl)-ureido]-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-(3-indan-5-yl-ureido)-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-[3-(2-phenyl-cyclopropyl)-ureido]-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-(3-adamantan-1-yl-ureido)-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-(3-biphenyl-4-yl-ureido)-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-[3-(4-phenoxy-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-[3-(4-nitro-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-(3-cyclohexyl-ureido)-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-(3-benzo[1,3]dioxol-5-yl-ureido)-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-[3-(2-fluoro-benzyl)-ureido]-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-[3-(4-methyl-benzyl)-ureido]-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-(3-phenethyl-ureido)-ureido]-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-[3-(3,4,5-trimethoxy-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-(3-ethyl-thioureido)-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-(3-isopropyl-thioureido)-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-[3-(4-nitro-phenyl)-thioureido]-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-(3-phenyl-thioureido)-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-[3-(4-trifluoromethoxy-phenyl)-thioureido]-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-{3-[4-(2,2,2-trifluoro-ethyl)-phenyl]-thioureido}-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-[3-(4-methoxy-phenyl)-thioureido]-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-ylmethanesulfonylamino)-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-(thiophene-2-sulfonylamino)-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-(4-trifluoromethoxy-benzenesulfonylamino)-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-(4-*tert*-butyl-benzenesulfonylamino)-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-(4-chloro-benzenesulfonylamino)-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-(4-methoxy-benzenesulfonylamino)-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-(quinoline-6-sulfonylamino)-propionic acid cyanoethyl-amide,

3-(1*H*-Indol-3-yl)-2-benzenesulfonylamino-propionic acid cyanoethyl-amide,

1-Methyl-1*H*-indole-2-carboxylic acid [1-(cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-amide

2-Propyl-pentanoic acid [1-(cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-amide,

1-Methyl-cyclopropanecarboxylic acid [1-(cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-amide,

Thiophene-2-carboxylic acid [1-(cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-amide,

N-[1-(Cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-3-trifluoromethyl-benzamide,
Biphenyl-2-carboxylic acid [1-(cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-amide,
4-Acetylamino-*N*-[1-(cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-benzamide,
3-(1*H*-indol-3-yl)-2-(2-1*H*-indol-3-yl-acetylamino)-propionic acid cyanoethyl-amide,
3-(1*H*-Indol-3-yl)-2-(3-1*H*-indol-3-yl-propionylamino)-propionic acid cyanoethyl-amide,
N-[1-(Cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-4-(1*H*-indol-3-yl)-butyramide,
N-[1-(Cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-benzamide,
3-Chloromethyl-*N*-[1-(cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-benzamide,
4-Chloromethyl-*N*-[1-(cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-benzamide,
N-[1-(Cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-2-fluoro-benzamide,
N-[1-(Cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-2-nitro-benzamide,
N-[1-(Cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-acrylamide,
3-(1*H*-Indol-3-yl)-2,2-dimethyl-propionic acid cyanoethyl-amide,
3-(1*H*-Indol-3-yl)-2-(2-methoxy-acetylamino)-propionic acid cyanoethyl-amide,
N-[1-(Cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-oxalamic acid methyl ester,
N-[1-(Cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-phthalamic acid,
N-[1-(Cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-succinamic acid,
3-[1-(Cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethylcarbamoyl]-acrylic acid,
[1-(Cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-carbamic acid isobutyl ester,
[1-(Cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-carbamic acid butyl ester,
[1-(Cyanomethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-carbamic acid cyanomethyl ester,
[1-(Cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-carbamic acid cyanomethyl ester,
[1-(Cyanomethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-carbamic acid but-3-enyl ester,
[1-(Cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-carbamic acid but-3-enyl ester,
[1-(Cyanomethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-carbamic acid 2-isopropyl-5-methyl-cyclohexyl ester,
[1-(Cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-carbamic acid 2-isopropyl-5-methyl-cyclohexyl ester,
[1-(Cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-carbamic acid hexyl ester,
[1-(Cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-carbamic acid *tert*-butyl ester,
[1-(Cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-carbamic acid methyl ester,
[1-(Cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-carbamic acid ethyl ester,
[1-(Cyanoethyl-carbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-carbamic acid 9*H*-fluoren-9-ylmethylester,
3-(4-Hydroxy-phenyl)-2-acetylamino-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(4-trifluoromethyl-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(4-trifluoromethylsulfanyl-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(4-trifluoromethoxy-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(4-cyano-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-(3-benzyl-ureido)-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-(3-o-tolyl-ureido)-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(*S*)-(1-phenyl-ethyl)-ureido]-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(2,6-dimethyl-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(3-methyl-benzyl)-ureido]-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(1,1,3,3-tetramethyl-butyl)-ureido]-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-(3-indan-5-yl-ureido)-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(2-phenyl-cyclopropyl)-ureido]-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-(3-adamantan-1-yl-ureido)-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-(3-biphenyl-4-yl-ureido)-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(4-phenoxy-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(4-nitro-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-(3-cyclohexyl-ureido)-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-(3-benzo[1,3]dioxol-5-yl-ureido)-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(2-fluoro-benzyl)-ureido]-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(4-methyl-benzyl)-ureido]-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-(3-phenethyl-ureido) -ureido]-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(3,4,5-trimethoxy-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-(3-ethyl-thioureido)-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-(3-isopropyl-thioureido)-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(4-nitro-phenyl)-thioureido]-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-(3-phenyl-thioureido)-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(4-trifluoromethoxy-phenyl)-thioureido]-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-{3-[4-(2,2,2-trifluoro-ethyl)-phenyl]-thioureido}-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(4-methoxy-phenyl)-thioureido]-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-ylmethanesulfonylamino)-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-(thiophene-2-sulfonylamino)-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-(4-trifluoromethoxy-benzenesulfonylamino)-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-(4-*tert*-butyl-benzenesulfonylamino)-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-(4-chloro-benzenesulfonylamino)-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-(4-methoxy-benzenesulfonylamino)-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-(quinoline-6-sulfonylamino)-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-benzenesulfonylamino-propionic acid cyanomethyl-amide,

1-Methyl-1H-indole-2-carboxylic acid [1-(cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-amide,

2-Propyl-pentanoic acid [1-(cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-amide,

1-Methyl-cyclopropanecarboxylic acid [1-(cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-amide,

Thiophene-2-carboxylic acid [1-(cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-amide,

N-[1-(Cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-3-trifluoromethyl-benzamide,

Biphenyl-2-carboxylic acid [1-(cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-amide,

4-Acetylamino-*N*-[1-(cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-benzamide,

3-(4-Hydroxy-phenyl)-2-(2-1*H*-indol-3-yl-acetylamino)-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-(3-1*H*-indol-3-yl-propionylamino)-propionic acid cyanomethyl-amide,

N-[1-(Cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-4-(1*H*-indol-3-yl)-butyramide,

N-[1-(Cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-benzamide,

3-Chloromethyl-*N*-[1-(cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-benzamide,

4-Chloromethyl-*N*-[1-(cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-benzamide,

N-[1-(Cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-2-fluoro-benzamide,

N-[1-(Cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-2-nitro-benzamide,

N-[1-(Cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-acrylamide,

3-(4-Hydroxy-phenyl)-2,2-dimethyl-propionic acid cyanomethyl-amide,

3-(4-Hydroxy-phenyl)-2-(2-methoxy-acetylamino)-propionic acid cyanomethyl-amide,

N-[1-(Cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-oxalamic acid methyl ester,

N-[1-(Cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-phthalamic acid,

N-[1-(Cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-succinamic acid,

3-[1-(Cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethylcarbamoyl]-acrylic acid,

[1-(Cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-carbamic acid isobutyl ester,

[1-(Cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-carbamic acid butyl ester,

[1-(Cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-carbamic acid hexyl ester,

[1-(Cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-carbamic acid *tert*-butyl ester,

[1-(Cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-carbamic acid methyl ester,

[1-(Cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-carbamic acid ethyl ester,

[1-(Cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-carbamic acid 9*H*-fluoren-9-ylmethyl ester,

3-(4-Hydroxy-phenyl)-2-acetylamino-propionic acid cyanoethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(4-trifluoromethyl-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(4-trifluoromethylsulfanyl-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(4-trifluoromethoxy-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(4-cyano-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-(4-Hydroxy-phenyl)-2-(3-benzyl-ureido)-propionic acid cyanoethyl-amide,

3-(4-Hydroxy-phenyl)-2-(3-o-tolyl-ureido)-propionic acid cyanoethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(*S*)-(1-phenyl-ethyl)-ureido]-propionic acid cyanoethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(2,6-dimethyl-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(3-methyl-benzyl)-ureido]-propionic acid cyanoethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(1,1,3,3-tetramethyl-butyl)-ureido]-propionic acid cyanoethyl-amide,

3-(4-Hydroxy-phenyl)-2-(3-indan-5-yl-ureido)-propionic acid cyanoethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(2-phenyl-cyclopropyl)-ureido]-propionic acid cyanoethyl-amide,

3-(4-Hydroxy-phenyl)-2-(3-adamantan-1-yl-ureido)-propionic acid cyanoethyl-amide,

3-(4-Hydroxy-phenyl)-2-(3-biphenyl-4-yl-ureido)-propionic acid cyanoethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(4-phenoxy-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(4-nitro-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-(4-Hydroxy-phenyl)-2-(3-cyclohexyl-ureido)-propionic acid cyanoethyl-amide,

3-(4-Hydroxy-phenyl)-2-(3-benzo[1,3]dioxol-5-yl-ureido)-propionic acid cyanoethyl-amide,

3-(4-Hydroxy-phenyl)-2-[3-(2-fluoro-benzyl)-ureido]-propionic acid cyanoethyl-amide,
3-(4-Hydroxy-phenyl)-2-[3-(4-methyl-benzyl)-ureido]-propionic acid cyanoethyl-amide,
3-(4-Hydroxy-phenyl)-2-(3-phenethyl-ureido) -ureido]-propionic acid cyanoethyl-amide,
3-(4-Hydroxy-phenyl)-2-[3-(3,4,5-trimethoxy-phenyl)-ureido]-propionic acid cyanoethyl-amide,
3-(4-Hydroxy-phenyl)-2-(3-ethyl-thioureido)-propionic acid cyanoethyl-amide,
3-(4-Hydroxy-phenyl)-2-(3-isopropyl-thioureido)-propionic acid cyanoethyl-amide,
3-(4-Hydroxy-phenyl)-2-[3-(4-nitro-phenyl)-thioureido]-propionic acid cyanoethyl-amide,
3-(4-Hydroxy-phenyl)-2-(3-phenyl-thioureido)-propionic acid cyanoethyl-amide,
3-(4-Hydroxy-phenyl)-2-[3-(4-trifluoromethoxy-phenyl)-thioureido]-propionic acid cyanoethyl-amide,
3-(4-Hydroxy-phenyl)-2-{3-[4-(2,2,2-trifluoro-ethyl)-phenyl]-thioureido}-propionic acid cyanoethyl-amide,
3-(4-Hydroxy-phenyl)-2-[3-(4-methoxy-phenyl)-thioureido]-propionic acid cyanoethyl-amide,
3-(4-Hydroxy-phenyl)-2-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-ylmethanesulfonylamino)-propionic acid cyanoethyl-amide,
3-(4-Hydroxy-phenyl)-2-(thiophene-2-sulfonylamino)-propionic acid cyanoethyl-amide,
3-(4-Hydroxy-phenyl)-2-(4-trifluoromethoxy-benzenesulfonylamino)-propionic acid cyanoethyl-amide,
3-(4-Hydroxy-phenyl)-2-(4-*tert*-butyl-benzenesulfonylamino)-propionic acid cyanoethyl-amide,
3-(4-Hydroxy-phenyl)-2-(4-chloro-benzenesulfonylamino)-propionic acid cyanoethyl-amide,
3-(4-Hydroxy-phenyl)-2-(4-methoxy-benzenesulfonylamino)-propionic acid cyanoethyl-amide,
3-(4-Hydroxy-phenyl)-2-(quinoline-6-sulfonylamino)-propionic acid cyanoethyl-amide,
3-(4-Hydroxy-phenyl)-2-benzenesulfonylamino-propionic acid cyanoethyl-amide,
1-Methyl-1H-indole-2-carboxylic acid [1-(cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-amide,
2-Propyl-pentanoic acid [1-(cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-amide,
1-Methyl-cyclopropanecarboxylic acid [1-(cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-amide,
Thiophene-2-carboxylic acid [1-(cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-amide,
N-[1-(Cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-3-trifluoromethyl-benzamide,
Biphenyl-2-carboxylic acid [1-(cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-amide,
4-Acetylamino-*N*-[1-(cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-benzamide,
3-(4-hydroxy-phenyl)-2-(2-1*H*-indol-3-yl-acetylamino)-propionic acid cyanoethyl-amide,
3-(4-Hydroxy-phenyl)-2-(3-1*H*-indol-3-yl-propionylamino)-propionic acid cyanoethyl-amide,

N-[1-(Cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-4-(1*H*-indol-3-yl)-butyramide,

N-[1-(Cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-benzamide,

3-Chloromethyl-*N*-[1-(cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-benzamide,

4-Chloromethyl-*N*-[1-(cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-benzamide,

N-[1-(Cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-2-fluoro-benzamide,

N-[1-(Cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-2-nitro-benzamide,

N-[1-(Cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-acrylamide,

3-(4-Hydroxy-phenyl)-2,2-dimethyl-propionic acid cyanoethyl-amide,

3-(4-Hydroxy-phenyl)-2-(2-methoxy-acetylamino)-propionic acid cyanoethyl-amide,

N-[1-(Cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-oxalamic acid methyl ester,

N-[1-(Cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-phthalamic acid,

N-[1-(Cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-succinamic acid,

3-[1-(Cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethylcarbamoyl]-acrylic acid,

[1-(Cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-carbamic acid isobutyl ester,

[1-(Cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-carbamic acid butyl ester,

[1-(Cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-carbamic acid cyanomethyl ester,

[1-(Cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-carbamic acid cyanomethyl ester,

[1-(Cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-carbamic acid but-3-enyl ester,

[1-(Cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-carbamic acid but-3-enyl ester,

[1-(Cyanomethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-carbamic acid 2-isopropyl-5-methyl-cyclohexyl ester,

[1-(Cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-carbamic acid 2-isopropyl-5-methyl-cyclohexyl ester,

[1-(Cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-carbamic acid hexyl ester,

[1-(Cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-carbamic acid *tert*-butyl ester,

[1-(Cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-carbamic acid methyl ester,

[1-(Cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-carbamic acid ethyl ester,

[1-(Cyanoethyl-carbamoyl)-2-(4-hydroxy-phenyl)-ethyl]-carbamic acid 9*H*-fluoren-9-ylmethylester,

3-Phenyl-2-acetylamino-propionic acid cyanomethyl-amide,

3-Phenyl-2-[3-(4-trifluoromethyl-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Phenyl-2-[3-(4-trifluoromethylsulfanyl-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Phenyl-2-[3-(4-trifluoromethoxy-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Phenyl-2-[3-(4-cyano-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Phenyl-2-(3-benzyl-ureido)-propionic acid cyanomethyl-amide,

3-Phenyl-2-(3-o-tolyl-ureido)-propionic acid cyanomethyl-amide,

3-Phenyl-2-[3-(*S*)-(1-phenyl-ethyl)-ureido]-propionic acid cyanomethyl-amide,

3-Phenyl-2-[3-(2,6-dimethyl-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Phenyl-2-[3-(3-methyl-benzyl)-ureido]-propionic acid cyanomethyl-amide,

3-Phenyl-2-[3-(1,1,3,3-tetramethyl-butyl)-ureido]-propionic acid cyanomethyl-amide,

3-Phenyl-2-(3-indan-5-yl-ureido)-propionic acid cyanomethyl-amide,

3-Phenyl-2-[3-(2-phenyl-cyclopropyl)-ureido]-propionic acid cyanomethyl-amide,

3-Phenyl-2-(3-adamantan-1-yl-ureido)-propionic acid cyanomethyl-amide,

3-Phenyl-2-(3-biphenyl-4-yl-ureido)-propionic acid cyanomethyl-amide,

3-Phenyl-2-[3-(4-phenoxy-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Phenyl-2-[3-(4-nitro-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Phenyl-2-(3-cyclohexyl-ureido)-propionic acid cyanomethyl-amide,

3-Phenyl-2-(3-benzo[1,3]dioxol-5-yl-ureido)-propionic acid cyanomethyl-amide,

3-Phenyl-2-[3-(2-fluoro-benzyl)-ureido]-propionic acid cyanomethyl-amide,

3-Phenyl-2-[3-(4-methyl-benzyl)-ureido]-propionic acid cyanomethyl-amide,

3-Phenyl-2-(3-phenethyl-ureido) -ureido]-propionic acid cyanomethyl-amide,

3-Phenyl-2-[3-(3,4,5-trimethoxy-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Phenyl-2-(3-ethyl-thioureido)-propionic acid cyanomethyl-amide,

3-Phenyl-2-(3-isopropyl-thioureido)-propionic acid cyanomethyl-amide,

3-Phenyl-2-[3-(4-nitro-phenyl)-thioureido]-propionic acid cyanomethyl-amide,

3-Phenyl-2-(3-phenyl-thioureido)-propionic acid cyanomethyl-amide,

3-Phenyl-2-[3-(4-trifluoromethoxy-phenyl)-thioureido]-propionic acid cyanomethyl-amide,

3-Phenyl-2-{3-[4-(2,2,2-trifluoro-ethyl)-phenyl]-thioureido}-propionic acid cyanomethyl-amide,

3-Phenyl-2-[3-(4-methoxy-phenyl)-thioureido]-propionic acid cyanomethyl-amide,

3-Phenyl-2-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-ylmethanesulfonylamino)-propionic acid cyanomethyl-amide,

3-Phenyl-2-(thiophene-2-sulfonylamino)-propionic acid cyanomethyl-amide,

3-Phenyl-2-(4-trifluoromethoxy-benzenesulfonylamino)-propionic acid cyanomethyl-amide,

3-Phenyl-2-(4-*tert*-butyl-benzenesulfonylamino)-propionic acid cyanomethyl-amide,

3-Phenyl-2-(4-chloro-benzenesulfonylamino)-propionic acid cyanomethyl-amide,

3-Phenyl-2-(4-methoxy-benzenesulfonylamino)-propionic acid cyanomethyl-amide,

3-Phenyl-2-(quinoline-6-sulfonylamino)-propionic acid cyanomethyl-amide,

3-Phenyl-2-benzenesulfonylamino-propionic acid cyanomethyl-amide,

1-Methyl-1H-indole-2-carboxylic acid [1-(cyanomethyl-carbamoyl)-2-phenyl-ethyl]-amide,

2-Propyl-pentanoic acid [1-(cyanomethyl-carbamoyl)-2-phenyl-ethyl]-amide,

1-Methyl-cyclopropanecarboxylic acid [1-(cyanomethyl-carbamoyl)-2-phenyl-ethyl]-amide,

Thiophene-2-carboxylic acid [1-(cyanomethyl-carbamoyl)-2-phenyl-ethyl]-amide,

N-[1-(Cyanomethyl-carbamoyl)-2-phenyl-ethyl]-3-trifluoromethyl-benzamide,

Biphenyl-2-carboxylic acid [1-(cyanomethyl-carbamoyl)-2-phenyl-ethyl]-amide,

4-Acetylamino-*N*-[1-(cyanomethyl-carbamoyl)-2-phenyl-ethyl]-benzamide,

3-Phenyl-2-(2-1*H*-indol-3-yl-acetylamino)-propionic acid cyanomethyl-amide,

3-Phenyl-2-(3-1*H*-indol-3-yl-propionylamino)-propionic acid cyanomethyl-amide,

N-[1-(Cyanomethyl-carbamoyl)-2-phenyl-ethyl]-4-(1*H*-indol-3-yl)-butyramide,

N-[1-(Cyanomethyl-carbamoyl)-2-phenyl-ethyl]-benzamide,

3-Chloromethyl-*N*-[1-(cyanomethyl-carbamoyl)-2-phenyl-ethyl]-benzamide,

4-Chloromethyl-*N*-[1-(cyanomethyl-carbamoyl)-2-phenyl-ethyl]-benzamide,

N-[1-(Cyanomethyl-carbamoyl)-2-phenyl-ethyl]-2-fluoro-benzamide,

N-[1-(Cyanomethyl-carbamoyl)-2-phenyl-ethyl]-2-nitro-benzamide,

N-[1-(Cyanomethyl-carbamoyl)-2-phenyl-ethyl]-acrylamide,

3-Phenyl-2,2-dimethyl-propionic acid cyanomethyl-amide,

3-Phenyl-2-(2-methoxy-acetylamino)-propionic acid cyanomethyl-amide,

N-[1-(Cyanomethyl-carbamoyl)-2-phenyl-ethyl]-oxalamic acid methyl ester,

N-[1-(Cyanomethyl-carbamoyl)-2-phenyl-ethyl]-phthalamic acid,

N-[1-(Cyanomethyl-carbamoyl)-2-phenyl-ethyl]-succinamic acid,

3-[1-(Cyanomethyl-carbamoyl)-2-phenyl-ethylcarbamoyl]-acrylic acid,

[1-(Cyanomethyl-carbamoyl)-2-phenyl-ethyl]-carbamic acid isobutyl ester,

[1-(Cyanomethyl-carbamoyl)-2-phenyl-ethyl]-carbamic acid butyl ester,

[1-(Cyanomethyl-carbamoyl)-2-phenyl-ethyl]-carbamic acid hexyl ester,

[1-(Cyanomethyl-carbamoyl)-2-phenyl-ethyl]-carbamic acid *tert*-butyl ester,

[1-(Cyanomethyl-carbamoyl)-2-phenyl-ethyl]-carbamic acid methyl ester,

[1-(Cyanomethyl-carbamoyl)-2-phenyl-ethyl]-carbamic acid ethyl ester,

[1-(Cyanomethyl-carbamoyl)-2-phenyl-ethyl]-carbamic acid 9*H*-fluoren-9-ylmethyl ester,

3-Phenyl-2-acetylamino-propionic acid cyanoethyl-amide,

3-Phenyl-2-[3-(4-trifluoromethyl-phenyl)-ureido]-propionic acid cyanoethyl-amide

3-Phenyl-2-[3-(4-trifluoromethylsulfanyl-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Phenyl-2-[3-(4-trifluoromethoxy-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Phenyl-2-[3-(4-cyano-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Phenyl-2-(3-benzyl-ureido)-propionic acid cyanoethyl-amide,

3-Phenyl-2-(3-o-tolyl-ureido)-propionic acid cyanoethyl-amide,

3-Phenyl-2-[3-(*S*)-(1-phenyl-ethyl)-ureido]-propionic acid cyanoethyl-amide,

3-Phenyl-2-[3-(2,6-dimethyl-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Phenyl-2-[3-(3-methyl-benzyl)-ureido]-propionic acid cyanoethyl-amide,

3-Phenyl-2-[3-(1,1,3,3-tetramethyl-butyl)-ureido]-propionic acid cyanoethyl-amide,

3-Phenyl-2-(3-indan-5-yl-ureido)-propionic acid cyanoethyl-amide,

3-Phenyl-2-[3-(2-phenyl-cyclopropyl)-ureido]-propionic acid cyanoethyl-amide,

3-Phenyl-2-(3-adamantan-1-yl-ureido)-propionic acid cyanoethyl-amide,

3-Phenyl-2-(3-biphenyl-4-yl-ureido)-propionic acid cyanoethyl-amide,

3-Phenyl-2-[3-(4-phenoxy-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Phenyl-2-[3-(4-nitro-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Phenyl-2-(3-cyclohexyl-ureido)-propionic acid cyanoethyl-amide,

3-Phenyl-2-(3-benzo[1,3]dioxol-5-yl-ureido)-propionic acid cyanoethyl-amide,

3-Phenyl-2-[3-(2-fluoro-benzyl)-ureido]-propionic acid cyanoethyl-amide,

3-Phenyl-2-[3-(4-methyl-benzyl)-ureido]-propionic acid cyanoethyl-amide,

3-Phenyl-2-(3-phenethyl-ureido) -ureido]-propionic acid cyanoethyl-amide,

3-Phenyl-2-[3-(3,4,5-trimethoxy-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Phenyl-2-(3-ethyl-thioureido)-propionic acid cyanoethyl-amide,

3-Phenyl-2-(3-isopropyl-thioureido)-propionic acid cyanoethyl-amide,

3-Phenyl-2-[3-(4-nitro-phenyl)-thioureido]-propionic acid cyanoethyl-amide,

3-Phenyl-2-(3-phenyl-thioureido)-propionic acid cyanoethyl-amide,

3-Phenyl-2-[3-(4-trifluoromethoxy-phenyl)-thioureido]-propionic acid cyanoethyl-amide,

3-Phenyl-2-{3-[4-(2,2,2-trifluoro-ethyl)-phenyl]-thioureido}-propionic acid cyanoethyl-amide,

3-Phenyl-2-[3-(4-methoxy-phenyl)-thioureido]-propionic acid cyanoethyl-amide,

3-Phenyl-2-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-ylmethanesulfonylamino)-propionic acid cyanoethyl-amide,

3-Phenyl-2-(thiophene-2-sulfonylamino)-propionic acid cyanoethyl-amide,

3-Phenyl-2-(4-trifluoromethoxy-benzenesulfonylamino)-propionic acid cyanoethyl-amide,

3-Phenyl-2-(4-*tert*-butyl-benzenesulfonylamino)-propionic acid cyanoethyl-amide,

3-Phenyl-2-(4-chloro-benzenesulfonylamino)-propionic acid cyanoethyl-amide,

3-Phenyl-2-(4-methoxy-benzenesulfonylamino)-propionic acid cyanoethyl-amide,

3-Phenyl-2-(quinoline-6-sulfonylamino)-propionic acid cyanoethyl-amide,

3-Phenyl-2-benzenesulfonylamino-propionic acid cyanoethyl-amide,

1-Methyl-1H-indole-2-carboxylic acid [1-(cyanoethyl-carbamoyl)-2-phenyl-ethyl]-amide,
2-Propyl-pentanoic acid [1-(cyanoethyl-carbamoyl)-2-phenyl-ethyl]-amide,
1-Methyl-cyclopropanecarboxylic acid [1-(cyanoethyl-carbamoyl)-2-phenyl-ethyl]-amide,
Thiophene-2-carboxylic acid [1-(cyanoethyl-carbamoyl)-2-phenyl-ethyl]-amide,
N-[1-(Cyanoethyl-carbamoyl)-2-phenyl-ethyl]-3-trifluoromethyl-benzamide,
Biphenyl-2-carboxylic acid [1-(cyanoethyl-carbamoyl)-2-phenyl-ethyl]-amide,
4-Acetylamino-*N*-[1-(cyanoethyl-carbamoyl)-2-phenyl-ethyl]-benzamide,
3-Phenyl-2-(2-1*H*-indol-3-yl-acetylamino)-propionic acid cyanoethyl-amide,
3-Phenyl-2-(3-1*H*-indol-3-yl-propionylamino)-propionic acid cyanoethyl-amide,
N-[1-(Cyanoethyl-carbamoyl)-2-phenyl-ethyl]-4-(1*H*-indol-3-yl)-butyramide,
N-[1-(Cyanoethyl-carbamoyl)-2-phenyl-ethyl]-benzamide,
3-Chloromethyl-*N*-[1-(cyanoethyl-carbamoyl)-2-phenyl-ethyl]-benzamide,
4-Chloromethyl-*N*-[1-(cyanoethyl-carbamoyl)-2-phenyl-ethyl]-benzamide,
N-[1-(Cyanoethyl-carbamoyl)-2-phenyl-ethyl]-2-fluoro-benzamide,
N-[1-(Cyanoethyl-carbamoyl)-2-phenyl-ethyl]-2-nitro-benzamide,
N-[1-(Cyanoethyl-carbamoyl)-2-phenyl-ethyl]-acrylamide,
3-Phenyl-2,2-dimethyl-propionic acid cyanoethyl-amide,
3-Phenyl-2-(2-methoxy-acetylamino)-propionic acid cyanoethyl-amide,
N-[1-(Cyanoethyl-carbamoyl)-2-phenyl-ethyl]-oxalamic acid methyl ester,
N-[1-(Cyanoethyl-carbamoyl)-2-phenyl-ethyl]-phthalamic acid,
N-[1-(Cyanoethyl-carbamoyl)-2-phenyl-ethyl]-succinamic acid,
3-[1-(Cyanoethyl-carbamoyl)-2-phenyl-ethylcarbamoyl]-acrylic acid,
[1-(Cyanoethyl-carbamoyl)-2-phenyl-ethyl]-carbamic acid isobutyl ester,
[1-(Cyanoethyl-carbamoyl)-2-phenyl-ethyl]-carbamic acid butyl ester,
[1-(Cyanomethyl-carbamoyl)-2-phenyl-ethyl]-carbamic acid cyanomethyl ester,
[1-(Cyanoethyl-carbamoyl)-2-phenyl-ethyl]-carbamic acid cyanomethyl ester,
[1-(Cyanomethyl-carbamoyl)-2-phenyl-ethyl]-carbamic acid but-3-enyl ester,
[1-(Cyanoethyl-carbamoyl)-2-phenyl-ethyl]-carbamic acid but-3-enyl ester,
[1-(Cyanomethyl-carbamoyl)-2-phenyl-ethyl]-carbamic acid 2-isopropyl-5-methyl-cyclohexyl ester,
[1-(Cyanoethyl-carbamoyl)-2-phenyl-ethyl]-carbamic acid 2-isopropyl-5-methyl-cyclohexyl ester,
[1-(Cyanoethyl-carbamoyl)-2-phenyl-ethyl]-carbamic acid hexyl ester,
[1-(Cyanoethyl-carbamoyl)-2-phenyl-ethyl]-carbamic acid *tert*-butyl ester,

[1-(Cyanoethyl-carbamoyl)-2-phenyl-ethyl]-carbamic acid methyl ester,

[1-(Cyanoethyl-carbamoyl)-2-phenyl-ethyl]-carbamic acid ethyl ester,

[1-(Cyanoethyl-carbamoyl)-2-phenyl-ethyl]-carbamic acid 9*H*-fluoren-9-ylmethylester,

3-Methylsulfanyl-2-acetylamino-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-[3-(4-trifluoromethyl-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-[3-(4-trifluoromethylsulfanyl-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-[3-(4-trifluoromethoxy-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-[3-(4-cyano-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-(3-benzyl-ureido)-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-(3-o-tolyl-ureido)-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-[3-(*S*)-(1-phenyl-ethyl)-ureido]-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-[3-(2,6-dimethyl-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-[3-(3-methyl-benzyl)-ureido]-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-[3-(1,1,3,3-tetramethyl-butyl)-ureido]-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-(3-indan-5-yl-ureido)-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-[3-(2-phenyl-cyclopropyl)-ureido]-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-(3-adamantan-1-yl-ureido)-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-(3-biphenyl-4-yl-ureido)-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-[3-(4-phenoxy-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-[3-(4-nitro-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-(3-cyclohexyl-ureido)-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-(3-benzo[1,3]dioxol-5-yl-ureido)-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-[3-(2-fluoro-benzyl)-ureido]-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-[3-(4-methyl-benzyl)-ureido]-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-(3-phenethyl-ureido) -ureido]-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-[3-(3,4,5-trimethoxy-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-(3-ethyl-thioureido)-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-(3-isopropyl-thioureido)-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-[3-(4-nitro-phenyl)-thioureido]-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-(3-phenyl-thioureido)-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-[3-(4-trifluoromethoxy-phenyl)-thioureido]-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-{3-[4-(2,2,2-trifluoro-ethyl)-phenyl]-thioureido}-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-[3-(4-methoxy-phenyl)-thioureido]-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-ylmethanesulfonylamino)-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-(thiophene-2-sulfonylamino)-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-(4-trifluoromethoxy-benzenesulfonylamino)-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-(4-*tert*-butyl-benzenesulfonylamino)-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-(4-chloro-benzenesulfonylamino)-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-(4-methoxy-benzenesulfonylamino)-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-(quinoline-6-sulfonylamino)-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-benzenesulfonylamino-propionic acid cyanomethyl-amide,

1-Methyl-1H-indole-2-carboxylic acid [1-(cyanomethyl-carbamoyl)-2-methylsulfanyl-ethyl]-amide,

2-Propyl-pentanoic acid [1-(cyanomethyl-carbamoyl)-2-methylsulfanyl-ethyl]-amide,

1-Methyl-cyclopropanecarboxylic acid [1-(cyanomethyl-carbamoyl)-2-methylsulfanyl-ethyl]-amide,

Thiophene-2-carboxylic acid [1-(cyanomethyl-carbamoyl)-2-methylsulfanyl-ethyl]-amide,

N-[1-(Cyanomethyl-carbamoyl)-2-methylsulfanyl-ethyl]-3-trifluoromethyl-benzamide,

Biphenyl-2-carboxylic acid [1-(cyanomethyl-carbamoyl)-2-methylsulfanyl-ethyl]-amide,

4-Acetylamino-*N*-[1-(cyanomethyl-carbamoyl)-2-methylsulfanyl-ethyl]-benzamide,

3-Methylsulfanyl-2-(2-1*H*-indol-3-yl-acetylamino)-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-(3-1*H*-indol-3-yl-propionylamino)-propionic acid cyanomethyl-amide,

N-[1-(Cyanomethyl-carbamoyl)-2-methylsulfanyl-ethyl]-4-(1*H*-indol-3-yl)-butyramide,

N-[1-(Cyanomethyl-carbamoyl)-2-methylsulfanyl-ethyl]-benzamide,

3-Chloromethyl-*N*-[1-(cyanomethyl-carbamoyl)-2-methylsulfanyl-ethyl]-benzamide,

4-Chloromethyl-*N*-[1-(cyanomethyl-carbamoyl)-2-methylsulfanyl-ethyl]-benzamide,

N-[1-(Cyanomethyl-carbamoyl)-2-methylsulfanyl-ethyl]-2-fluoro-benzamide,

N-[1-(Cyanomethyl-carbamoyl)-2-methylsulfanyl-ethyl]-2-nitro-benzamide,

N-[1-(Cyanomethyl-carbamoyl)-2-methylsulfanyl-ethyl]-acrylamide,

3-Methylsulfanyl-2,2-dimethyl-propionic acid cyanomethyl-amide,

3-Methylsulfanyl-2-(2-methoxy-acetylamino)-propionic acid cyanomethyl-amide,

N-[1-(Cyanomethyl-carbamoyl)-2-methylsulfanyl-ethyl]-oxalamic acid methyl ester,

N-[1-(Cyanomethyl-carbamoyl)-2-methylsulfanyl-ethyl]-phthalamic acid,

N-[1-(Cyanomethyl-carbamoyl)-2-methylsulfanyl-ethyl]-succinamic acid,

3-[1-(Cyanomethyl-carbamoyl)-2-methylsulfanyl-ethylcarbamoyl]-acrylic acid,

[1-(Cyanomethyl-carbamoyl)-2-methylsulfanyl-ethyl]-carbamic acid isobutyl ester,

[1-(Cyanomethyl-carbamoyl)-2-methylsulfanyl-ethyl]-carbamic acid butyl ester,

[1-(Cyanomethyl-carbamoyl)-2-methylsulfanyl-ethyl]-carbamic acid hexyl ester,

[1-(Cyanomethyl-carbamoyl)-2-methylsulfanyl-ethyl]-carbamic acid *tert*-butyl ester,

[1-(Cyanomethyl-carbamoyl)-2-methylsulfanyl-ethyl]-carbamic acid methyl ester,

[1-(Cyanomethyl-carbamoyl)-2-methylsulfanyl-ethyl]-carbamic acid ethyl ester,

[1-(Cyanomethyl-carbamoyl)-2-methylsulfanyl-ethyl]-carbamic acid 9*H*-fluoren-9-ylmethyl ester,

3-Methylsulfanyl-2-acetylamino-propionic acid cyanoethyl-amide,

3-Methylsulfanyl-2-[3-(4-trifluoromethyl-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Methylsulfanyl-2-[3-(4-trifluoromethylsulfanyl-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Methylsulfanyl-2-[3-(4-trifluoromethoxy-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Methylsulfanyl-2-[3-(4-cyano-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Methylsulfanyl-2-(3-benzyl-ureido)-propionic acid cyanoethyl-amide,

3-Methylsulfanyl-2-(3-o-tolyl-ureido)-propionic acid cyanoethyl-amide,

3-Methylsulfanyl-2-[3-(*S*)-(1-phenyl-ethyl)-ureido]-propionic acid cyanoethyl-amide,

3-Methylsulfanyl-2-[3-(2,6-dimethyl-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Methylsulfanyl-2-[3-(3-methyl-benzyl)-ureido]-propionic acid cyanoethyl-amide,

3-Methylsulfanyl-2-[3-(1,1,3,3-tetramethyl-butyl)-ureido]-propionic acid cyanoethyl-amide,

3-Methylsulfanyl-2-(3-indan-5-yl-ureido)-propionic acid cyanoethyl-amide,

3-Methylsulfanyl-2-[3-(2-phenyl-cyclopropyl)-ureido]-propionic acid cyanoethyl-amide,

3-Methylsulfanyl-2-(3-adamantan-1-yl-ureido)-propionic acid cyanoethyl-amide,

3-Methylsulfanyl-2-(3-biphenyl-4-yl-ureido)-propionic acid cyanoethyl-amide,

3-Methylsulfanyl-2-[3-(4-phenoxy-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Methylsulfanyl-2-[3-(4-nitro-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Methylsulfanyl-2-(3-cyclohexyl-ureido)-propionic acid cyanoethyl-amide,

3-Methylsulfanyl-2-(3-benzo[1,3]dioxol-5-yl-ureido)-propionic acid cyanoethyl-amide,

3-Methylsulfanyl-2-[3-(2-fluoro-benzyl)-ureido]-propionic acid cyanoethyl-amide,

3-Methylsulfanyl-2-[3-(4-methyl-benzyl)-ureido]-propionic acid cyanoethyl-amide,

3-Methylsulfanyl-2-(3-phenethyl-ureido) -ureido]-propionic acid cyanoethyl-amide,

3-Methylsulfanyl-2-[3-(3,4,5-trimethoxy-phenyl)-ureido]-propionic acid cyanoethyl-amide,
3-Methylsulfanyl-2-(3-ethyl-thioureido)-propionic acid cyanoethyl-amide,
3-Methylsulfanyl-2-(3-isopropyl-thioureido)-propionic acid cyanoethyl-amide,
3-Methylsulfanyl-2-[3-(4-nitro-phenyl)-thioureido]-propionic acid cyanoethyl-amide,
3-Methylsulfanyl-2-(3-phenyl-thioureido)-propionic acid cyanoethyl-amide,
3-Methylsulfanyl-2-[3-(4-trifluoromethoxy-phenyl)-thioureido]-propionic acid cyanoethyl-amide,
3-Methylsulfanyl-2-{3-[4-(2,2,2-trifluoro-ethyl)-phenyl]-thioureido}-propionic acid cyanoethyl-amide,
3-Methylsulfanyl-2-[3-(4-methoxy-phenyl)-thioureido]-propionic acid cyanoethyl-amide,
3-Methylsulfanyl-2-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-ylmethanesulfonylamino)-propionic acid cyanoethyl-amide,
3-Methylsulfanyl-2-(thiophene-2-sulfonylamino)-propionic acid cyanoethyl-amide,
3-Methylsulfanyl-2-(4-trifluoromethoxy-benzenesulfonylamino)-propionic acid cyanoethyl-amide,
3-Methylsulfanyl-2-(4-*tert*-butyl-benzenesulfonylamino)-propionic acid cyanoethyl-amide,
3-Methylsulfanyl-2-(4-chloro-benzenesulfonylamino)-propionic acid cyanoethyl-amide,
3-Methylsulfanyl-2-(4-methoxy-benzenesulfonylamino)-propionic acid cyanoethyl-amide,
3-Methylsulfanyl-2-(quinoline-6-sulfonylamino)-propionic acid cyanoethyl-amide,
3-Methylsulfanyl-2-benzenesulfonylamino-propionic acid cyanoethyl-amide,
1-Methyl-1H-indole-2-carboxylic acid [1-(cyanoethyl-carbamoyl)-2-methylsulfanyl-ethyl]-amide,
2-Propyl-pentanoic acid [1-(cyanoethyl-carbamoyl)-2-methylsulfanyl-ethyl]-amide,
1-Methyl-cyclopropanecarboxylic acid [1-(cyanoethyl-carbamoyl)-2-methylsulfanyl-ethyl]-amide,
Thiophene-2-carboxylic acid [1-(cyanoethyl-carbamoyl)-2-methylsulfanyl-ethyl]-amide,
N-[1-(Cyanoethyl-carbamoyl)-2-methylsulfanyl-ethyl]-3-trifluoromethyl-benzamide,
Biphenyl-2-carboxylic acid [1-(cyanoethyl-carbamoyl)-2-methylsulfanyl-ethyl]-amide,
4-Acetylamino-*N*-[1-(cyanoethyl-carbamoyl)-2-methylsulfanyl-ethyl]-benzamide,
3-Methylsulfanyl-2-(2-1*H*-indol-3-yl-acetylamino)-propionic acid cyanoethyl-amide,
3-Methylsulfanyl-2-(3-1*H*-indol-3-yl-propionylamino)-propionic acid cyanoethyl-amide,
N-[1-(Cyanoethyl-carbamoyl)-2-methylsulfanyl-ethyl]-4-(1*H*-indol-3-yl)-butyramide,
N-[1-(Cyanoethyl-carbamoyl)-2-methylsulfanyl-ethyl]-benzamide,
3-Chloromethyl-*N*-[1-(cyanoethyl-carbamoyl)-2-methylsulfanyl-ethyl]-benzamide,

4-Chloromethyl-*N*-[1-(cyanoethyl-carbamoyl)-2-methylsulfanyl-ethyl]-benzamide,
N-[1-(Cyanoethyl-carbamoyl)-2-methylsulfanyl-ethyl]-2-fluoro-benzamide,
N-[1-(Cyanoethyl-carbamoyl)-2-methylsulfanyl-ethyl]-2-nitro-benzamide,
N-[1-(Cyanoethyl-carbamoyl)-2-methylsulfanyl-ethyl]-acrylamide,
3-Methylsulfanyl-2,2-dimethyl-propionic acid cyanoethyl-amide,
3-Methylsulfanyl-2-(2-methoxy-acetylamino)-propionic acid cyanoethyl-amide,
N-[1-(Cyanoethyl-carbamoyl)-2-methylsulfanyl-ethyl]-oxalamic acid methyl ester,
N-[1-(Cyanoethyl-carbamoyl)-2-methylsulfanyl-ethyl]-phthalamic acid,
N-[1-(Cyanoethyl-carbamoyl)-2-methylsulfanyl-ethyl]-succinamic acid,
3-[1-(Cyanoethyl-carbamoyl)-2-methylsulfanyl-ethylcarbamoyl]-acrylic acid,
[1-(Cyanoethyl-carbamoyl)-2-methylsulfanyl-ethyl]-carbamic acid isobutyl ester,
[1-(Cyanoethyl-carbamoyl)-2-methylsulfanyl-ethyl]-carbamic acid butyl ester,
[1-(Cyanomethyl-carbamoyl)-2-methylsulfanyl-ethyl]-carbamic acid cyanomethyl ester,
[1-(Cyanoethyl-carbamoyl)-2-methylsulfanyl-ethyl]-carbamic acid cyanomethyl ester,
[1-(Cyanomethyl-carbamoyl)-2-methylsulfanyl-ethyl]-carbamic acid but-3-enyl ester,
[1-(Cyanoethyl-carbamoyl)-2-methylsulfanyl-ethyl]-carbamic acid but-3-enyl ester,
[1-(Cyanomethyl-carbamoyl)-2-methylsulfanyl-ethyl]-carbamic acid 2-isopropyl-5-methyl-cyclohexyl ester,
[1-(Cyanoethyl-carbamoyl)-2-methylsulfanyl-ethyl]-carbamic acid 2-isopropyl-5-methyl-cyclohexyl ester,
[1-(Cyanoethyl-carbamoyl)-2-methylsulfanyl-ethyl]-carbamic acid hexyl ester,
[1-(Cyanoethyl-carbamoyl)-2-methylsulfanyl-ethyl]-carbamic acid *tert*-butyl ester,
[1-(Cyanoethyl-carbamoyl)-2-methylsulfanyl-ethyl]-carbamic acid methyl ester,
[1-(Cyanoethyl-carbamoyl)-2-methylsulfanyl-ethyl]-carbamic acid ethyl ester,
[1-(Cyanoethyl-carbamoyl)-2-methylsulfanyl-ethyl]-carbamic acid 9*H*-fluoren-9-ylmethylester,
3-Methanesulfonyl-2-acetylamino-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-[3-(4-trifluoromethyl-phenyl)-ureido]-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-[3-(4-trifluoromethylsulfanyl-phenyl)-ureido]-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-[3-(4-trifluoromethoxy-phenyl)-ureido]-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-[3-(4-cyano-phenyl)-ureido]-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-(3-benzyl-ureido)-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-(3-o-tolyl-ureido)-propionic acid cyanomethyl-amide,

3-Methanesulfonyl-2-[3-(*S*)-(1-phenyl-ethyl)-ureido]-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-[3-(2,6-dimethyl-phenyl)-ureido]-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-[3-(3-methyl-benzyl)-ureido]-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-[3-(1,1,3,3-tetramethyl-butyl)-ureido]-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-(3-indan-5-yl-ureido)-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-[3-(2-phenyl-cyclopropyl)-ureido]-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-(3-adamantan-1-yl-ureido)-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-(3-biphenyl-4-yl-ureido)-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-[3-(4-phenoxy-phenyl)-ureido]-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-[3-(4-nitro-phenyl)-ureido]-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-(3-cyclohexyl-ureido)-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-(3-benzo[1,3]dioxol-5-yl-ureido)-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-[3-(2-fluoro-benzyl)-ureido]-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-[3-(4-methyl-benzyl)-ureido]-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-(3-phenethyl-ureido) -ureido]-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-[3-(3,4,5-trimethoxy-phenyl)-ureido]-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-(3-ethyl-thioureido)-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-(3-isopropyl-thioureido)-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-[3-(4-nitro-phenyl)-thioureido]-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-(3-phenyl-thioureido)-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-[3-(4-trifluoromethoxy-phenyl)-thioureido]-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-{3-[4-(2,2,2-trifluoro-ethyl)-phenyl]-thioureido}-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-[3-(4-methoxy-phenyl)-thioureido]-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-ylmethanesulfonylamino)-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-(thiophene-2-sulfonylamino)-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-(4-trifluoromethoxy-benzenesulfonylamino)-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-(4-*tert*-butyl-benzenesulfonylamino)-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-(4-chloro-benzenesulfonylamino)-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-(4-methoxy-benzenesulfonylamino)-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-(quinoline-6-sulfonylamino)-propionic acid cyanomethyl-amide,

3-Methanesulfonyl-2-benzenesulfonylamino-propionic acid cyanomethyl-amide,
1-Methyl-1H-indole-2-carboxylic acid [1-(cyanomethyl-carbamoyl)-2-methanesulfonyl-ethyl]-amide,
2-Propyl-pentanoic acid [1-(cyanomethyl-carbamoyl)-2-methanesulfonyl-ethyl]-amide,
1-Methyl-cyclopropanecarboxylic acid [1-(cyanomethyl-carbamoyl)-2-methanesulfonyl-ethyl]-amide,
Thiophene-2-carboxylic acid [1-(cyanomethyl-carbamoyl)-2-methanesulfonyl-ethyl]-amide,
N-[1-(Cyanomethyl-carbamoyl)-2-methanesulfonyl-ethyl]-3-trifluoromethyl-benzamide,
Biphenyl-2-carboxylic acid [1-(cyanomethyl-carbamoyl)-2-methanesulfonyl-ethyl]-amide,
4-Acetylamino-*N*-[1-(cyanomethyl-carbamoyl)-2-methanesulfonyl-ethyl]-benzamide,
3-Methanesulfonyl-2-(2-1*H*-indol-3-yl-acetylamino)-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-(3-1*H*-indol-3-yl-propionylamino)-propionic acid cyanomethyl-amide,
N-[1-(Cyanomethyl-carbamoyl)-2-methanesulfonyl-ethyl]-4-(1*H*-indol-3-yl)-butyramide,
N-[1-(Cyanomethyl-carbamoyl)-2-methanesulfonyl-ethyl]-benzamide,
3-Chloromethyl-*N*-[1-(cyanomethyl-carbamoyl)-2-methanesulfonyl-ethyl]-benzamide,
4-Chloromethyl-*N*-[1-(cyanomethyl-carbamoyl)-2-methanesulfonyl-ethyl]-benzamide,
N-[1-(Cyanomethyl-carbamoyl)-2-methanesulfonyl-ethyl]-2-fluoro-benzamide,
N-[1-(Cyanomethyl-carbamoyl)-2-methanesulfonyl-ethyl]-2-nitro-benzamide,
N-[1-(Cyanomethyl-carbamoyl)-2-methanesulfonyl-ethyl]-acrylamide,
3-Methanesulfonyl-2,2-dimethyl-propionic acid cyanomethyl-amide,
3-Methanesulfonyl-2-(2-methoxy-acetylamino)-propionic acid cyanomethyl-amide,
N-[1-(Cyanomethyl-carbamoyl)-2-methanesulfonyl-ethyl]-oxalamic acid methyl ester,
N-[1-(Cyanomethyl-carbamoyl)-2-methanesulfonyl-ethyl]-phthalamic acid,
N-[1-(Cyanomethyl-carbamoyl)-2-methanesulfonyl-ethyl]-succinamic acid,
3-[1-(Cyanomethyl-carbamoyl)-2-methanesulfonyl-ethylcarbamoyl]-acrylic acid,
[1-(Cyanomethyl-carbamoyl)-2-methanesulfonyl-ethyl]-carbamic acid isobutyl ester,
[1-(Cyanomethyl-carbamoyl)-2-methanesulfonyl-ethyl]-carbamic acid butyl ester,
[1-(Cyanomethyl-carbamoyl)-2-methanesulfonyl-ethyl]-carbamic acid hexyl ester,
[1-(Cyanomethyl-carbamoyl)-2-methanesulfonyl-ethyl]-carbamic acid *tert*-butyl ester,
[1-(Cyanomethyl-carbamoyl)-2-methanesulfonyl-ethyl]-carbamic acid methyl ester,
[1-(Cyanomethyl-carbamoyl)-2-methanesulfonyl-ethyl]-carbamic acid ethyl ester,
[1-(Cyanomethyl-carbamoyl)-2-methanesulfonyl-ethyl]-carbamic acid 9*H*-fluoren-9-ylmethyl ester,
3-Methanesulfonyl-2-acetylamino-propionic acid cyanoethyl-amide,

3-Methanesulfonyl-2-[3-(4-trifluoromethyl-phenyl)-ureido]-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-[3-(4-trifluoromethylsulfanyl-phenyl)-ureido]-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-[3-(4-trifluoromethoxy-phenyl)-ureido]-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-[3-(4-cyano-phenyl)-ureido]-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-(3-benzyl-ureido)-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-(3-o-tolyl-ureido)-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-[3-(*S*)-(1-phenyl-ethyl)-ureido]-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-[3-(2,6-dimethyl-phenyl)-ureido]-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-[3-(3-methyl-benzyl)-ureido]-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-[3-(1,1,3,3-tetramethyl-butyl)-ureido]-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-(3-indan-5-yl-ureido)-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-[3-(2-phenyl-cyclopropyl)-ureido]-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-(3-adamantan-1-yl-ureido)-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-(3-biphenyl-4-yl-ureido)-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-[3-(4-phenoxy-phenyl)-ureido]-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-[3-(4-nitro-phenyl)-ureido]-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-(3-cyclohexyl-ureido)-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-(3-benzo[1,3]dioxol-5-yl-ureido)-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-[3-(2-fluoro-benzyl)-ureido]-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-[3-(4-methyl-benzyl)-ureido]-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-(3-phenethyl-ureido) -ureido]-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-[3-(3,4,5-trimethoxy-phenyl)-ureido]-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-(3-ethyl-thioureido)-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-(3-isopropyl-thioureido)-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-[3-(4-nitro-phenyl)-thioureido]-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-(3-phenyl-thioureido)-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-[3-(4-trifluoromethoxy-phenyl)-thioureido]-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-{3-[4-(2,2,2-trifluoro-ethyl)-phenyl]-thioureido}-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-[3-(4-methoxy-phenyl)-thioureido]-propionic acid cyanoethyl-amide,
3-Methanesulfonyl-2-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-ylmethanesulfonylamino)-propionic acid cyanoethyl-amide,

3-Methanesulfonyl-2-(thiophene-2-sulfonylamino)-propionic acid cyanoethyl-amide,

3-Methanesulfonyl-2-(4-trifluoromethoxy-benzenesulfonylamino)-propionic acid cyanoethyl-amide,

3-Methanesulfonyl-2-(4-*tert*-butyl-benzenesulfonylamino)-propionic acid cyanoethyl-amide,

3-Methanesulfonyl-2-(4-chloro-benzenesulfonylamino)-propionic acid cyanoethyl-amide,

3-Methanesulfonyl-2-(4-methoxy-benzenesulfonylamino)-propionic acid cyanoethyl-amide,

3-Methanesulfonyl-2-(quinoline-6-sulfonylamino)-propionic acid cyanoethyl-amide,

3-Methanesulfonyl-2-benzenesulfonylamino-propionic acid cyanoethyl-amide,

1-Methyl-1H-indole-2-carboxylic acid [1-(cyanoethyl-carbamoyl)-2-methanesulfonyl-ethyl]-amide,

2-Propyl-pentanoic acid [1-(cyanoethyl-carbamoyl)-2-methanesulfonyl-ethyl]-amide,

1-Methyl-cyclopropanecarboxylic acid [1-(cyanoethyl-carbamoyl)-2-methanesulfonyl-ethyl]-amide,

Thiophene-2-carboxylic acid [1-(cyanoethyl-carbamoyl)-2-methanesulfonyl-ethyl]-amide,

N-[1-(Cyanoethyl-carbamoyl)-2-methanesulfonyl-ethyl]-3-trifluoromethyl-benzamide,

Biphenyl-2-carboxylic acid [1-(cyanoethyl-carbamoyl)-2-methanesulfonyl-ethyl]-amide,

4-Acetylamino-*N*-[1-(cyanoethyl-carbamoyl)-2-methanesulfonyl-ethyl]-benzamide,

3-Methanesulfonyl-2-(2-1*H*-indol-3-yl-acetylamino)-propionic acid cyanoethyl-amide,

3-Methanesulfonyl-2-(3-1*H*-indol-3-yl-propionylamino)-propionic acid cyanoethyl-amide,

N-[1-(Cyanoethyl-carbamoyl)-2-methanesulfonyl-ethyl]-4-(1*H*-indol-3-yl)-butyramide,

N-[1-(Cyanoethyl-carbamoyl)-2-methanesulfonyl-ethyl]-benzamide,

3-Chloromethyl-*N*-[1-(cyanoethyl-carbamoyl)-2-methanesulfonyl-ethyl]-benzamide,

4-Chloromethyl-*N*-[1-(cyanoethyl-carbamoyl)-2-methanesulfonyl-ethyl]-benzamide,

N-[1-(Cyanoethyl-carbamoyl)-2-methanesulfonyl-ethyl]-2-fluoro-benzamide,

N-[1-(Cyanoethyl-carbamoyl)-2-methanesulfonyl-ethyl]-2-nitro-benzamide,

N-[1-(Cyanoethyl-carbamoyl)-2-methanesulfonyl-ethyl]-acrylamide,

3-Methanesulfonyl-2,2-dimethyl-propionic acid cyanoethyl-amide,

3-Methanesulfonyl-2-(2-methoxy-acetylamino)-propionic acid cyanoethyl-amide,

N-[1-(Cyanoethyl-carbamoyl)-2-methanesulfonyl-ethyl]-oxalamic acid methyl ester,

N-[1-(Cyanoethyl-carbamoyl)-2-methanesulfonyl-ethyl]-phthalamic acid,

N-[1-(Cyanoethyl-carbamoyl)-2-methanesulfonyl-ethyl]-succinamic acid,

3-[1-(Cyanoethyl-carbamoyl)-2-methanesulfonyl-ethylcarbamoyl]-acrylic acid,

[1-(Cyanoethyl-carbamoyl)-2-methanesulfonyl-ethyl]-carbamic acid isobutyl ester,

[1-(Cyanoethyl-carbamoyl)-2-methanesulfonyl-ethyl]-carbamic acid butyl ester,

[1-(Cyanomethyl-carbamoyl)-2-methanesulfonyl-ethyl]-carbamic acid cyanomethyl ester,

[1-(Cyanoethyl-carbamoyl)-2-methanesulfonyl-ethyl]-carbamic acid cyanomethyl ester,

[1-(Cyanomethyl-carbamoyl)-2-methanesulfonyl-ethyl]-carbamic acid but-3-enyl ester,

[1-(Cyanoethyl-carbamoyl)-2-methanesulfonyl-ethyl]-carbamic acid but-3-enyl ester,

[1-(Cyanomethyl-carbamoyl)-2-methanesulfonyl-ethyl]-carbamic acid 2-isopropyl-5-methyl-cyclohexyl ester,

[1-(Cyanoethyl-carbamoyl)-2-methanesulfonyl-ethyl]-carbamic acid 2-isopropyl-5-methyl-cyclohexyl ester,

[1-(Cyanoethyl-carbamoyl)-2-methanesulfonyl-ethyl]-carbamic acid hexyl ester,

[1-(Cyanoethyl-carbamoyl)-2-methanesulfonyl-ethyl]-carbamic acid *tert*-butyl ester,

[1-(Cyanoethyl-carbamoyl)-2-methanesulfonyl-ethyl]-carbamic acid methyl ester,

[1-(Cyanoethyl-carbamoyl)-2-methanesulfonyl-ethyl]-carbamic acid ethyl ester,

[1-(Cyanoethyl-carbamoyl)-2-methanesulfonyl-ethyl]-carbamic acid 9*H*-fluoren-9-ylmethylester,

3-Naphthalen-2-yl-2-acetylamino-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-[3-(4-trifluoromethyl-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-[3-(4-trifluoromethylsulfanyl-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-[3-(4-trifluoromethoxy-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-[3-(4-cyano-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-(3-benzyl-ureido)-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-(3-o-tolyl-ureido)-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-[3-(*S*)-(1-phenyl-ethyl)-ureido]-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-[3-(2,6-dimethyl-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-[3-(3-methyl-benzyl)-ureido]-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-[3-(1,1,3,3-tetramethyl-butyl)-ureido]-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-(3-indan-5-yl-ureido)-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-[3-(2-phenyl-cyclopropyl)-ureido]-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-(3-adamantan-1-yl-ureido)-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-(3-biphenyl-4-yl-ureido)-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-[3-(4-phenoxy-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-[3-(4-nitro-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-(3-cyclohexyl-ureido)-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-(3-benzo[1,3]dioxol-5-yl-ureido)-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-[3-(2-fluoro-benzyl)-ureido]-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-[3-(4-methyl-benzyl)-ureido]-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-(3-phenethyl-ureido) -ureido]-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-[3-(3,4,5-trimethoxy-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-(3-ethyl-thioureido)-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-(3-isopropyl-thioureido)-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-[3-(4-nitro-phenyl)-thioureido]-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-(3-phenyl-thioureido)-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-[3-(4-trifluoromethoxy-phenyl)-thioureido]-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-{3-[4-(2,2,2-trifluoro-ethyl)-phenyl]-thioureido}-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-[3-(4-methoxy-phenyl)-thioureido]-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-ylmethanesulfonylamino)-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-(thiophene-2-sulfonylamino)-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-(4-trifluoromethoxy-benzenesulfonylamino)-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-(4-*tert*-butyl-benzenesulfonylamino)-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-(4-chloro-benzenesulfonylamino)-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-(4-methoxy-benzenesulfonylamino)-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-(quinoline-6-sulfonylamino)-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-benzenesulfonylamino-propionic acid cyanomethyl-amide,

1-Methyl-1H-indole-2-carboxylic acid [1-(cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-amide,

2-Propyl-pentanoic acid [1-(cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-amide,

1-Methyl-cyclopropanecarboxylic acid [1-(cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-amide,

Thiophene-2-carboxylic acid [1-(cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-amide,

N-[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-3-trifluoromethyl-benzamide,

Biphenyl-2-carboxylic acid [1-(cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-amide,

4-Acetylamino-*N*-[1-(cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-benzamide,

3-Naphthalen-2-yl-2-(2-1*H*-indol-3-yl-acetylamino)-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-(3-1*H*-indol-3-yl-propionylamino)-propionic acid cyanomethyl-amide,

N-[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-4-(1*H*-indol-3-yl)-butyramide,

N-[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-benzamide,

3-Chloromethyl-*N*-[1-(cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-benzamide,

4-Chloromethyl-*N*-[1-(cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-benzamide,

N-[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-2-fluoro-benzamide,

N-[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-2-nitro-benzamide,

N-[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-acrylamide,

3-Naphthalen-2-yl-2,2-dimethyl-propionic acid cyanomethyl-amide,

3-Naphthalen-2-yl-2-(2-methoxy-acetylamino)-propionic acid cyanomethyl-amide,

N-[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-oxalamic acid methyl ester,

N-[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-phthalamic acid,

N-[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-succinamic acid,

3-[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethylcarbamoyl]-acrylic acid,"

[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid isobutyl ester,

[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid butyl ester,

[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid hexyl ester,

[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid *tert*-butyl ester,

[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid methyl ester,

[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid ethyl ester,

[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid 9*H*-fluoren-9-ylmethyl ester,

3-Naphthalen-2-yl-2-acetylamino-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-[3-(4-trifluoromethyl-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-[3-(4-trifluoromethylsulfanyl-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-[3-(4-trifluoromethoxy-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-[3-(4-cyano-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-(3-benzyl-ureido)-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-(3-o-tolyl-ureido)-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-[3-(*S*)-(1-phenyl-ethyl)-ureido]-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-[3-(2,6-dimethyl-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-[3-(3-methyl-benzyl)-ureido]-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-[3-(1,1,3,3-tetramethyl-butyl)-ureido]-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-(3-indan-5-yl-ureido)-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-[3-(2-phenyl-cyclopropyl)-ureido]-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-(3-adamantan-1-yl-ureido)-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-(3-biphenyl-4-yl-ureido)-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-[3-(4-phenoxy-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-[3-(4-nitro-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-(3-cyclohexyl-ureido)-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-(3-benzo[1,3]dioxol-5-yl-ureido)-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-[3-(2-fluoro-benzyl)-ureido]-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-[3-(4-methyl-benzyl)-ureido]-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-(3-phenethyl-ureido) -ureido]-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-[3-(3,4,5-trimethoxy-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-(3-ethyl-thioureido)-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-(3-isopropyl-thioureido)-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-[3-(4-nitro-phenyl)-thioureido]-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-(3-phenyl-thioureido)-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-[3-(4-trifluoromethoxy-phenyl)-thioureido]-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-{3-[4-(2,2,2-trifluoro-ethyl)-phenyl]-thioureido}-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-[3-(4-methoxy-phenyl)-thioureido]-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-ylmethanesulfonylamino)-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-(thiophene-2-sulfonylamino)-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-(4-trifluoromethoxy-benzenesulfonylamino)-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-(4-*tert*-butyl-benzenesulfonylamino)-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-(4-chloro-benzenesulfonylamino)-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-(4-methoxy-benzenesulfonylamino)-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-(quinoline-6-sulfonylamino)-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-benzenesulfonylamino-propionic acid cyanoethyl-amide,

1-Methyl-1H-indole-2-carboxylic acid [1-(cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-amide,

2-Propyl-pentanoic acid [1-(cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-amide,

1-Methyl-cyclopropanecarboxylic acid [1-(cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-amide,

Thiophene-2-carboxylic acid [1-(cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-amide,

N-[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-3-trifluoromethyl-benzamide,

Biphenyl-2-carboxylic acid [1-(cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-amide,

4-Acetylamino-*N*-[1-(cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-benzamide,

3-Naphthalen-2-yl-2-(2-1*H*-indol-3-yl-acetylamino)-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-(3-1*H*-indol-3-yl-propionylamino)-propionic acid cyanoethyl-amide,

N-[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-4-(1*H*-indol-3-yl)-butyramide,

N-[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-benzamide,

3-Chloromethyl-*N*-[1-(cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-benzamide,

4-Chloromethyl-*N*-[1-(cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-benzamide,

N-[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-2-fluoro-benzamide,

N-[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-2-nitro-benzamide,

N-[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-acrylamide,

3-Naphthalen-2-yl-2,2-dimethyl-propionic acid cyanoethyl-amide,

3-Naphthalen-2-yl-2-(2-methoxy-acetylamino)-propionic acid cyanoethyl-amide,

N-[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-oxalamic acid methyl ester,

N-[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-phthalamic acid,

N-[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-succinamic acid,

3-[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethylcarbamoyl]-acrylic acid,

[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid isobutyl ester,

[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid butyl ester,

[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid cyanomethyl ester,

[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid cyanomethyl ester,

[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid but-3-enyl ester,

[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid but-3-enyl ester,

[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid 2-isopropyl-5-methyl-cyclohexyl ester,

[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid 2-isopropyl-5-methyl-cyclohexyl ester,

[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid hexyl ester,

[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid *tert*-butyl ester,

[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid methyl ester,

[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid ethyl ester,

[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid 9*H*-fluoren-9-ylmethylester,

3-Benzo[b]thiophen-3-yl-2-acetylamino-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(4-trifluoromethyl-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(4-trifluoromethylsulfanyl-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(4-trifluoromethoxy-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(4-cyano-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(3-benzyl-ureido)-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(3-*o*-tolyl-ureido)-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(*S*)-(1-phenyl-ethyl)-ureido]-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(2,6-dimethyl-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(3-methyl-benzyl)-ureido]-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(1,1,3,3-tetramethyl-butyl)-ureido]-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(3-indan-5-yl-ureido)-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(2-phenyl-cyclopropyl)-ureido]-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(3-adamantan-1-yl-ureido)-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(3-biphenyl-4-yl-ureido)-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(4-phenoxy-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(4-nitro-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(3-cyclohexyl-ureido)-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(3-benzo[1,3]dioxol-5-yl-ureido)-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(2-fluoro-benzyl)-ureido]-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(4-methyl-benzyl)-ureido]-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(3-phenethyl-ureido) -ureido]-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(3,4,5-trimethoxy-phenyl)-ureido]-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(3-ethyl-thioureido)-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(3-isopropyl-thioureido)-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(4-nitro-phenyl)-thioureido]-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(3-phenyl-thioureido)-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(4-trifluoromethoxy-phenyl)-thioureido]-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-{3-[4-(2,2,2-trifluoro-ethyl)-phenyl]-thioureido}-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(4-methoxy-phenyl)-thioureido]-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-ylmethanesulfonylamino)-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(thiophene-2-sulfonylamino)-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(4-trifluoromethoxy-benzenesulfonylamino)-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(4-*tert*-butyl-benzenesulfonylamino)-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(4-chloro-benzenesulfonylamino)-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(4-methoxy-benzenesulfonylamino)-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(quinoline-6-sulfonylamino)-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-benzenesulfonylamino-propionic acid cyanomethyl-amide,

1-Methyl-1H-indole-2-carboxylic acid [2-benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-amide,

2-Propyl-pentanoic acid [2-benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-amide,

1-Methyl-cyclopropanecarboxylic acid [2-benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-amide,

Thiophene-2-carboxylic acid [2-benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-amide,

N-[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-3-trifluoromethyl-benzamide,

Biphenyl-2-carboxylic acid [2-benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-amide,

4-Acetylamino-*N*-[2-benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-benzamide,

3-Benzo[b]thiophen-3-yl-2-(2-1*H*-indol-3-yl-acetylamino)-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(3-1*H*-indol-3-yl-propionylamino)-propionic acid cyanomethyl-amide,

N-[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-4-(1*H*-indol-3-yl)-butyramide,

N-[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-benzamide,

N-[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-acrylamide,

N-[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-acrylamide,

3-Benzo[b]thiophen-3-yl-2,2-dimethyl-propionic acid cyanomethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(2-methoxy-acetylamino)-propionic acid cyanomethyl-amide,

N-[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-oxalamic acid methyl ester,

N-[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-phthalamic acid,

N-[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-succinamic acid,

3-[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethylcarbamoyl]-acrylic acid,

[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-carbamic acid isobutyl ester,

[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-carbamic acid butyl ester,

[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-carbamic acid cyanomethyl ester,

[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-carbamic acid but-3-enyl ester,

[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-carbamic acid 2-isopropyl-5-methyl-cyclohexyl ester,

[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-carbamic acid hexyl ester,

[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-carbamic acid tert-butyl ester,

[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-carbamic acid methyl ester,

[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)--ethyl]-carbamic acid ethyl ester,

[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-carbamic acid 9*H*-fluoren-9-ylmethyl ester,

3-Benzo[b]thiophen-3-yl-2-acetylamino-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(4-trifluoromethyl-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(4-trifluoromethylsulfanyl-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(4-trifluoromethoxy-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(4-cyano-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(3-benzyl-ureido)-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(3-*o*-tolyl-ureido)-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(*S*)-(1-phenyl-ethyl)-ureido]-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(2,6-dimethyl-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(3-methyl-benzyl)-ureido]-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(1,1,3,3-tetramethyl-butyl)-ureido]-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(3-indan-5-yl-ureido)-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(2-phenyl-cyclopropyl)-ureido]-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(3-adamantan-1-yl-ureido)-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(3-biphenyl-4-yl-ureido)-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(4-phenoxy-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(4-nitro-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(3-cyclohexyl-ureido)-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(3-benzo[1,3]dioxol-5-yl-ureido)-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(2-fluoro-benzyl)-ureido]-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(4-methyl-benzyl)-ureido]-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(3-phenethyl-ureido) -ureido]-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(3,4,5-trimethoxy-phenyl)-ureido]-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(3-ethyl-thioureido)-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(3-isopropyl-thioureido)-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(4-nitro-phenyl)-thioureido]-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(3-phenyl-thioureido)-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(4-trifluoromethoxy-phenyl)-thioureido]-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-{3-[4-(2,2,2-trifluoro-ethyl)-phenyl]-thioureido}-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-[3-(4-methoxy-phenyl)-thioureido]-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-ylmethanesulfonylamino)-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(thiophene-2-sulfonylamino)-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(4-trifluoromethoxy-benzenesulfonylamino)-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(4-*tert*-butyl-benzenesulfonylamino)-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(4-chloro-benzenesulfonylamino)-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(4-methoxy-benzenesulfonylamino)-propionic acid cyanoethyl-amide,

3-Benzo[b]thiophen-3-yl-2-(quinoline-6-sulfonylamino)-propionic acid cyanoethyl-amide,
3-Benzo[b]thiophen-3-yl-2-benzenesulfonylamino-propionic acid cyanoethyl-amide,
1-Methyl-1H-indole-2-carboxylic acid [2-benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-amide,
2-Propyl-pentanoic acid [2-benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-amide,
1-Methyl-cyclopropanecarboxylic acid [2-benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-amide,
Thiophene-2-carboxylic acid [2-benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-amide,
N-[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-3-trifluoromethyl-benzamide,
Biphenyl-2-carboxylic acid [2-benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-amide,
4-Acetylamino-*N*-[2-benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-benzamide,
3-Benzo[b]thiophen-3-yl-2-(2-1*H*-indol-3-yl-acetylamino)-propionic acid cyanoethyl-amide,
3-Benzo[b]thiophen-3-yl-2-(3-1*H*-indol-3-yl-propionylamino)-propionic acid cyanoethyl-amide,
N-[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-4-(1*H*-indol-3-yl)-butyramide,
N-[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-benzamide,
3-Chloromethyl-*N*-[2-benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-benzamide,
4-Chloromethyl-*N*-[2-benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-benzamide,
N-[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-2-fluoro-benzamide,
N-[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-2-nitro-benzamide,
3-Chloromethyl-*N*-[2-benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-benzamide,
4-Chloromethyl-*N*-[2-benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-benzamide,
N-[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-2-fluoro-benzamide,
N-[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-2-nitro-benzamide,
3-Benzo[b]thiophen-3-yl-2,2-dimethyl-propionic acid cyanoethyl-amide,
3-Benzo[b]thiophen-3-yl-2-(2-methoxy-acetylamino)-propionic acid cyanoethyl-amide,
N-[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-oxalamic acid methyl ester,
N-[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-phthalamic acid,
N-[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-succinamic acid,
3-[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethylcarbamoyl]-acrylic acid,
[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-carbamic acid isobutyl ester,

1-Cyanomethyl-pyrrolidine-2-carboxylic acid carbamoylmethyl-amide
1-Cyanomethyl-pyrrolidine-2-carboxylic acid (1-carbamoyl-2-methyl-propyl)-amide
1-Cyanomethyl-pyrrolidine-2-carboxylic acid (1-carbamoyl-2-hydroxy-ethyl)-amide

1-Cyanomethyl-pyrrolidine-2-carboxylic acid (1-carbamoyl-4-guanidino-butyl)-amide

1-Cyanomethyl-pyrrolidine-2-carboxylic acid (1-carbamoyl-2-phenyl-ethyl)-amide

1-Cyanomethyl-pyrrolidine-2-carboxylic acid [1-carbamoyl-2-(1H-indol-3-yl)-ethyl]-amide

1-Cyanomethyl-pyrrolidine-2-carboxylic acid [1-carbamoyl-2-(4-hydroxy-phenyl)-ethyl]-amide

3-[(1-Cyanomethyl-pyrrolidine-2-carbonyl)-amino]-succinamic acid

D-1-Cyanomethyl-pyrrolidine-2-carboxylic acid (1-carbamoyl-3-methyl-butyl)-amide

1-Cyanomethyl-pyrrolidine-2-carboxylic acid (1-carbamoyl-cyclohexyl)-amide

1-Cyanomethyl-pyrrolidine-2-carboxylic acid [1-carbamoyl-2-(4-trifluoromethyl-benzylsulfanyl)-ethyl]-amide

1-Cyanomethyl-pyrrolidine-2-carboxylic acid [1-carbamoyl-2-(4-fluoro-benzylsulfanyl)-ethyl]-amide

1-Cyanomethyl-pyrrolidine-2-carboxylic acid [1-carbamoyl-2-(4-fluoro-phenylmethanesulfonyl)-ethyl]-amide

1-Cyanomethyl-pyrrolidine-2-carboxylic acid (3-carbamoyl-phenyl)-amide

1-Cyanomethyl-pyrrolidine-2-carboxylic acid [1-carbamoyl-2-(1-methyl-1H-imidazol-4-yl)-ethyl]-amide

1-Cyanomethyl-pyrrolidine-2-carboxylic acid (1-carbamoyl-2-pyridin-4-yl-ethyl)-amide

1-Cyanomethyl-pyrrolidine-2-carboxylic acid (1-carbamoyl-3-methyl-butyl)-amide

1-Cyanomethyl-pyrrolidine-2-carboxylic acid methyl ester

1-Cyanomethyl-pyrrolidine-2-carboxylic acid

N-(2-Cyanoethyl)-4-(4-dimethylamino-phenylazo)-benzenesulfonamide

N-(2-Cyanoethyl)-4-trifluoromethoxy-benzenesulfonamide

4-tert-Butyl-N-(2-cyanoethyl)-benzenesulfonamide

4-Bromo-N-(2-cyanoethyl)-benzenesulfonamide

4-Chloro-N-(2-cyanoethyl)-benzenesulfonamide

N-(2-Cyanoethyl)-4-methoxy-benzenesulfonamide

N-[4-(2-Cyanoethyl-sulfamoyl)-phenyl]-acetamide

N-(2-Cyanoethyl)-4-methyl-benzenesulfonamide

N-(2-Cyanoethyl)-benzenesulfonamide

N-(2-Cyanoethyl)-C-phenyl-methanesulfonamide

C,C,C-Trichloro-N-(2-cyanoethyl)-methanesulfonamide

Butane-1-sulfonic acid (2-cyanoethyl)-amide

Naphthalene-1-sulfonic acid (2-cyanoethyl)-amide

Octane-1-sulfonic acid (2-cyanoethyl)-amide

N-(2-Cyanoethyl)-2,4,6-triisopropyl-benzenesulfonamide

N-(2-Cyanoethyl)-2-trifluoromethyl-benzenesulfonamide

N-[5-(2-Cyanoethyl-sulfamoyl)-4-methyl-thiazol-2-yl]-acetamide

2-Bromo-N-(2-cyanoethyl)-benzenesulfonamide

N-(2-Cyanoethyl)-2,4,6-trimethyl-benzenesulfonamide

Thiophene-2-sulfonic acid (2-cyanoethyl)-amide

N-(2-Cyanoethyl)-3-nitro-benzenesulfonamide

1-(2-Cyanoethyl)-3-(4-nitro-phenyl)-thiourea

1-(2-Cyano 1-(2-Cyano-ethyl)-3-phenyl-thioureaethyl)-3-phenyl-thiourea

1-(2-Cyanoethyl)-3-(4-trifluoromethoxy-phenyl)-thiourea

1-(2-Cyanoethyl)-3-(4-methylsulfanyl-phenyl)-thiourea

1-(2-Cyanoethyl)-3-(3,4,5-trimethoxy-phenyl)-thiourea

1-(2-Cyanoethyl)-3-naphthalen-1-yl-thiourea

1-Benzyl-3-(2-cyanoethyl)-thiourea

1-Acetyl-3-(2-cyanoethyl)-thiourea

1-(4-Azido-phenyl)-3-(2-cyanoethyl)-thiourea

1-(2-Cyanoethyl)-3-(3-cyano-phenyl)-thiourea

1-(2-Cyano1-(2-Cyano-ethyl)-3-(4-ethyl-phenyl)-thioureaethyl)-3-(4-ethyl-phenyl)-thiourea

1-(2-Cyano1-(2-Cyano-ethyl)-3-(4-cyano-phenyl)-thioureaethyl)-3-(4-cyano-phenyl)-thiourea

1-Carbamoylmethyl-pyrrolidine-2-carboxylic acid (1-carbamoyl-3-methyl-butyl)-amide1-(2-Cyanoethyl)-3-pyridin-4-yl-thiourea

1-(2-Cyanoethyl)-3-(2,3,4-trifluoro-phenyl)-thiourea

1-(2-Cyanoethyl)-3-(2,6-difluoro-phenyl)-thiourea

1-(4-Bromo-phenyl)-3-(2-cyanoethyl)-thiourea

1-(2-Cyanoethyl)-3-(4-methoxy-phenyl)-thiourea

1-(2-Cyanoethyl)-3-m-tolyl-thiourea

1-(2-Cyanoethyl)-3-p-tolyl-thiourea

1-(2-Cyanoethyl)-3-cyclohexyl-urea

1-(2-Cyanoethyl)-3-o-tolyl-urea

1-(2-Cyanoethyl)-3-(2-methoxy-phenyl)-urea

[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-carbamic acid butyl ester,

[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-carbamic acid cyanomethyl ester,
[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-carbamic acid but-3-enyl ester,
[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-carbamic acid 2-isopropyl-5-methyl-cyclohexyl ester,
[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-carbamic acid hexyl ester,
[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-carbamic acid tert-butyl ester,
[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-carbamic acid methyl ester,
[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-carbamic acid ethyl ester,
[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-carbamic acid 9*H*-fluoren-9-ylmethylester,
or a pharmaceutically acceptable salt, solvate, hydrate or prodrug thereof.

Even more preferred compounds according to the present invention are those mentioned in any of the tables herein and those further disclosed and/or characterized in the examples.

The problem underlying the present invention is also solved by the subject matter of the independent claims. Preferred embodiments are described in the dependent claims.

As used herein, each of the following terms, used alone or in conjunction with other terms, are defined as follows (except where noted to the contrary):

The term "alkyl" refers to a saturated aliphatic radical containing from one to fourteen carbon atoms or a mono- or polyunsaturated aliphatic hydrocarbon radical containing from two to twelve carbon atoms, containing at least one double and triple bound, respectively. "Alkyl" refers to both branched and unbranched alkyl groups. Preferred alkyl groups are straight chain alkyl groups containing from one to eight carbon atoms. More preferred alkyl groups are straight chain alkyl groups containing from one to six carbon atoms and branched alkyl groups containing from three to six carbon atoms. It should be understood that any combination term using an "alk" or "alkyl" prefix refers to analogs according to the above definition of "alkyl". For example, terms such as "alkoxy", "alkylthio" refer to alkyl group linked to a second group via an oxygen or sulfur atom. "Alkanoyl" refers to an alkyl group linked to a carbonyl group (C=O). "Substituted alkyl" refers to alkyl groups straight or branched further bearing one or more substituents. One substituent also means mono-substituted and more substitutents mean poly-substituted. It should

be understood that any combination term using a "substituted alkyl" prefix refers to analogs according to the above definition of "substituted alkyl". For example, a term such as "substituted alkylaryl" refers to substituted alkyl group linked to an aryl group.

The term "lower alkyl" as used herein is preferably any alkyl as disclosed herein, whereby the alkyl comprises one to six, preferably one to five, and more preferably one or four C-atoms.

The term "cycloalkyl" refers to the cyclic analog of an alkyl group, as defined above, optionally unsaturated and/or substituted. Preferred cycloalkyl groups are saturated cycloalkyl groups, more particularly those containing from three to eight carbon atoms, and even more preferably three to six carbon atoms. "Substituted cycloalkyl" refers to cycloalkyl groups further bearing one or more substituents. "Mono–unsaturated cycloalkyl" refers to cycloalkyl containing one double bond or one triple bond. "Poly–unsaturated cycloalkyl" refers to cycloalkyl containing at least two double bonds or two triple bonds or a combination of at least one double bond and one triple bond.

The term "alkenyl" refers to an unsaturated hydrocarbon group containing at least one carbon-carbon double bond, including straight-chain, branched-chain, and cyclic groups. Preferred alkenyl groups have one to twelve carbons. More preferred alkenyl groups have one to six carbons. "Substituted alkenyl" refers to alkenyl groups further bearing one or more substitutents.

The term "cycloalkenyl" refers to the cyclic analog of an alkenyl group, as defined above, optionally substituted. Preferred cycloalkenyl groups are containing from four to eight carbon atoms. "Substituted cycloalkenyl" refers to cycloalkenyl groups further bearing one or more substituents. "Mono–unsaturated cycloalkenyl" refers to cycloalkenyl containing one double bond. "Poly–unsaturated cycloalkenyl" refers to cycloalkenyl containing at least two double bonds.

The term "alkynyl" refers to an unsaturated hydrocarbon group containing at least one carbon-carbon triple bond, including straight-chain, branched-chain, and cyclic groups. Preferred alkynyl groups have one to twelve carbons. More preferred alkynyl groups have one to six carbons. "Substituted alkynyl" refers to alkynyl groups further bearing one or more substitutents.

The term "aryl" refers to aromatic groups having in the range of 6 to 14 carbon atoms and "substituted aryl" refers to aryl groups further bearing one or more substituents. It should be understood that any combination term using an "ar" or "aryl" prefix refers to analogs according to the above definition of "aryl". For example, a term such as "aryloxy" refers to aryl group linked to a second group via an oxygen.

Each of the above defined "alkyl", "cycloalkyl", and "aryl" shall be understood to include their halogenated analogs, whereby the halogenated analogs may comprise one or several halogen atoms. The halogenated analogs thus comprise any halogen radical as defined in the following.

The term "halo" refers to a halogen radical selected from the group comprising fluoro, chloro, bromo and iodo. Preferred halo groups are fluoro, chloro and bromo.

The term "heteroaryl" refers to a stable 5 to 8 membered, preferably 5 or 6 membered monocyclic or 8 to 11 membered bicyclic aromatic heterocycle radical. Each heterocycle consists of carbon atoms and from 1 to 4 heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur. The heterocycle may be attached by any atom of the cycle which results in the creation of a stable structure. Preferred heteroaryl radicals as used herein include, for example, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolizinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, indazolyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, purinyl, quinolizinyl, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, naphthridinyl, pteridinyl, carbazolyl, acridinyl, phenazinyl, phenothiazinyl and phenoxazinyl. "Substituted heteroaryl" refers to heteroaryl groups further bearing one or more substituents.

The term "heterocyclyl" refers to a stable 5 to 8 membered, preferably 5 or 6 membered monocyclic or 8 to 11 membered bicyclic heterocycle radical which may be either saturated or unsaturated, and is non-aromatic. Each heterocycle consists of carbon atom(s) and from 1 to 4 heteroatoms selected from the group consisting of nitrogen, oxygen and sulfur. The heterocycle may be attached by any atom of the cycle, which preferably results in the creation of a stable structure. Preferred heterocycle radicals as used herein include, for example, pyrrolinyl, pyrrolidinyl, pyrazolinyl, pyrazolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, pyranyl, thiopyranyl, piperazinyl, indolinyl, azetidinyl, tetrahydropyranyl, tetrahydrothiopyranyl,

tetrahydrofuranyl, hexahydropyrimidinyl, hexahydropyridazinyl, 1,4,5,6-tetrahydropyrimidin-2-ylamine, dihydro-oxazolyl, 1,2-thiazinanyl-1,1-dioxide, 1,2,6-thiadiazinanyl-1,1-dioxide, isothiazolidinyl-1,1-dioxide and imidazolidinyl-2,4-dione. "Mono–unsaturated heterocyclyl" refers to heterocyclyl containing one double bond or one triple bond. "Poly–unsaturated heterocyclyl" refers to heterocyclyl containing at least two double bonds or two triple bonds or a combination of at least one double bond and one triple bond.

"Substituted heterocyclyl" refers to heterocyclyl groups further bearing one or more substituents.

The terms "heterocyclyl", "heteroaryl" and "aryl", when associated with another moiety, unless otherwise specified, shall have the same meaning as given above. For example, "aroyl" refers to phenyl or naphthyl linked to a carbonyl group (C=O).

Each aryl or heteroaryl unless otherwise specified includes its partially or fully hydrogenated derivative. For example, quinolinyl may include decahydroquinolinyl and tetrahydroquinolinyl, naphthyl may include its hydrogenated derivatives such as tetrahydranaphthyl.

As used herein above and throughout this application, "nitrogen" or "N" and "sulfur" or "S" include any oxidized form of nitrogen such as nitrone, N-oxide and sulfur such as sulfoxide, sulfone and the quaternized form of any basic nitrogen such as HCl or TFA salts.

As used herein a wording defining the limits of a range of length such as e. g. "1 to 5" means any integer from 1 to 5, i. e. 1, 2, 3, 4 and 5. In other words, any range defined by two integers explicitly mentioned is meant to comprise any integer defining said limits and any integer comprised in said range.

As used herein the term substituted shall mean that one or more H atom of the group or compound which is substituted, is replaced by a different atom, a group of atoms, a molecule or a molecule moiety. Such atom, group of atoms, molecule or molecule moiety is also referred to herein as substituent.

The substituent can be selected from the group comprising hydroxy, alkoxy, mercapto, cycloalkyl, heterocyclic, aryl, heteroaryl, aryloxy, halogen, trifluoromethyl, difluoromethyl,

cyano, nitrone, amino, amido, -C(O)H, acyl, oxyacyl, carboxyl, carbamate, sulfonyl, sulphonamide and sulfuryl. Any of the substituents may be substituted itself by any of the aforementioned substituents. This applies preferably to cycloalkyl, heterocylic, aryl, heteroaryl and aryloxy. It is also preferred that alkoxy and mercapto are those of a lower alkyl group. It is to be acknowledged that any of the definition provided herein also applies to any substituent. In preferred embodiments of the present invention a substituent can also be selected from the group comprising K, L1, L2, R^a to R^o and R^1 to R^{29}, U, W, Y and Z.

As used herein =T can mean in any embodiment of the various aspects of the present invention that with =T is selected from electron withdrawing groups, whereby preferably the electron withdrawing groups are selected from =O, =N–R^1, =N–CN, =N–NO_2 and =CH–NO_2, and =S,

It is within the present invention that any thiourea moieties and derivates therefrom, particularly those described herein, can, in principle be replaced by a cyanoguanidine moiety or residue and respective derivates therefrom as described in J. Med. Chem 1977, 20, 901 – 906. In Addition to being weakly basic cyanoguanidine and thiourea are also weakly acidic and both are therefore neutral and weakly amphoteric compounds. Cyanoguanidine is also similar to thiourea in its geometry since both are planar structures with almost identical C-N bond lengths and bond angles. Another property common to thioureas and cyanoguanidines is conformational isomerism resulting from restricted C-N bond rotation. Cyanoguanidine and thiourea are similar in their hydrophilicity and hydrogen-bonding properties; they have comparably low octanol-water partition coefficients (P) and are both reasonably soluble in water.

As used herein in connection with an embodiment of the various aspects of the present invention the term "each and independently selected from a group" or "are independently from each other selected from the group" refers to two or more atoms, groups, substituents, moieties or whatsoever and describes that the single atom, group etc. mentioned can be selected from the group. The wording used is a truncation which avoids unnecessary repetition as otherwise for each of the atoms, groups etc. the same group definition would have to be repeated.

As used herein in connection with an embodiment of the various aspects of the present invention the term "each and individually absent" refers to two or more atoms, groups, substituents, moieties or whatsoever and describes that the single atom, group etc. mentioned can be absent

regardless whether any of the other atoms, groups etc. mentioned is absent. The wording used is a truncation which avoids unnecessary repetition as otherwise for each of the atoms, groups etc. the fact that it may be absent in an embodiment of the invention would have to be repeated.

In connection with the present invention some groups such as, e.g., $-(CR^eR^d)-$ are repeated, i.e. are repeatedly present in a compound according to the present invention. Typically such repetition occurs in such a manner that, e.g., $-(CR^eR^d)-$ is repeated one or several times. In case, e.g., $-(CR^eR^d)-$ is repeated one time which means that there are two consecutive groups of $-(CR^eR^d)-$, these two forms of $-(C^eR^d)-$ can be either the same or they may be different in a different embodiment which means that either R^e or R^d or both of them are different between said two $-(CR^eR^d)-$ groups. If there are three or more of these groups such as , e.g., $-(CR^eR^d)-$, it is possible that all of them are different or only some or different whereas others are the same in the sense defined above. Any permutation for the arrangement for such identical or different groups is within the present invention.

It is to be acknowledged and within the present invention that any radical, group, moiety or substituent as used herein can be linked or inserted in any orientation into any of the respective formulae or compounds disclosed or described herein.

As used herein in connection with an embodiment of the various aspects of the present invention the term referring to a group, substituent, moiety, spacer or the like specifying that it "can be inserted in any orientation into any of the preceding formulae" means that the group etc. can be attached to another atom, group, substitutent, moiety, spacer or the like of any of the compounds according to the present invention or any of the formulae disclosed herein via any of its ends and in particular through any of the atoms arranged at the ends of said group, substituent, moiety, spacer or the like.

This applies particularly to asymmetric groups or radicals which can thus be, in principle, inserted in any orientation.

It is within the present invention that the features of the various embodiments of the present invention can be realized either alone or in combination with the features of any other embodiment(s) of the present invention. Thus any combination of an/the individual feature or the combination of features of an embodiment of the present invention with an/the individual

feature(s) or the combination of features of any other embodiment(s), either alone or in combination with other embodiments, shall be disclosed by the present specification.

It is to be understood that the term group as used herein in preferred embodiments, is also to mean or comprise radical and/or diradical or any further radical having more than two free valences. It will be acknowledged by the ones skilled in the art that the various radicals or groups are linked, preferably covalently linked, to another radical, group, component or moiety of the compound. Therefore, it is appropriate to understand that such groups are regarded as radicals. It will also acknowledged that a radical can, in principle, have either one, two, three or four free valences in case of a carbon atom, for binding to or with other such radicals, groups, compounds or moieties. It is also acknowledged by the ones skilled in the art that the number of free valences thus provided defines the number of radicals with which the first radical can form a covalent bonding.

Any of the compounds according to the present invention may be subject to or result from a chemical transformation. Such transformation converts the compound or the respective precursor thereof. The chemical transformation is selected from the group comprising hydrolysis, oxidation and reduction. Preferably, such chemical transformation is an enzymatic transformation. More preferably, the transformation is carried out *in vitro* or *in vivo*. This kind of chemical transformation preferably happens to a prodrug which as such or the product thereof may be pharmaceutically active in the meaning of the present invention.

The compounds according to the present invention, the pharmaceutical salts thereof, products and any derivatives, may be modified such that the *in vivo* and/or *in vitro* enzymatic degradation, such as proteolytic degradation, of said compounds is reduced or prevented. Generally, this is done through the incorporation of synthetic amino acids, derivatives, or substituents into the respective compound. Preferably, only one non-naturally occurring amino acid or amino acid side chain is incorporated into the compound, such that the targeting of the inhibitor of the appropriate enzyme is not significantly affected. However, some embodiments that use longer compounds according to the present invention containing a number of targeting residues may tolerate more than one synthetic derivative. In addition, non-naturally occurring amino acid substituents may be designed to mimic the binding of the naturally occurring side chain to the targeted enzyme, such that more than one synthetic substituent is tolerated. Alternatively, peptide isosteres are used to reduce or prevent the compound's degradation. The resistance of the thus

modified compound may be tested against the variety of known commercially available enzymes *in vitro* to determine the stability against enzymatic, preferably proteolytic, stability. Promising candidates may then be routinely screened in animal models, for example using labeled compounds as described herein, to determine the *in vivo* stability and efficacy.

In this embodiment, the resistance of the modified nonproteolytic reactive enzyme inhibitors may be tested against a variety of known commercially available nonproteolytic reactive enzymes *in vitro* to determine their proteolytic stability. Promising candidates may then be routinely screened in animal models, for example using labelled inhibitors, to determine the *in vivo* stability and efficacy.

In a still further aspect the compounds according to the present invention have at least one amino acid side chain. Preferably, the amino acid side chain is in the (S) or L-configuration or in the (R) or D-configuration. Of said configurations the (S) or L-configuration is particularly preferred.

In a preferred embodiment, the compound or pharmaceutically acceptable salt or product of said compound according to the present invention comprises one or more non-naturally occurring amino acids or amino acid side chains. Alternatively or in addition thereto, said compounds may comprise a peptide isostere.

In a further aspect the present invention is related to the use of a compound according to any of the aspects of the present invention as an inhibitor to or for a rotamase.

In an embodiment the rotamase regulates a part of the cell cycle.

In a preferred embodiment the rotamase regulates a part of the cell cycle, whereby preferably the part of the cell cycle is mitosis.

In an even more preferred embodiment the rotamase is a mammalian rotamase, preferably a human rotamase, more preferably hPin1.

In a further aspect the present invention is related to the use of the compounds according to the present invention as a pharmaceutical or in a pharmaceutical composition or for the manufacture

of such pharmaceutical composition which is preferably for the prophylaxis and/or treatment of a disease, whereby preferably the disease involves a rotamase, whereby the rotamase is a mammalian rotamase, preferably a human rotamase, more preferably hPin1.

In connection with the further aspect of the present invention related to the use of any of the aforementioned compounds according to the present invention as an inhibitor to rotamases the following will be acknowledged by the one skilled in the art. In view of the characteristics of the compounds according to the present invention to be active as an inhibitor of (a) rotamase(s), it is sufficient that the respective compound is at least suitable to inhibit at least one rotamase. The compounds according to the present invention which may be used as inhibitors, are also referred to as rotamase inhibitors herein.

Rotamases as such are known in the art and, for example, described in the introductory part of this specification which is incorporated by reference. Rotamases as used herein shall preferably mean cyclophilins, FK-506 binding proteins and the rotamases of the Pin1/parvulin class. The Pin1/parvulin family includes Pins 1, PinL/parvulin, dodo, and Esl/Pft1. Suitable assays to determine whether a compound is suitable to inhibit a rotamase are known to the one skilled in the art and also described in the present examples. Basically, a rotamase is provided the activity of which or non-activity of which may be determined. A candidate inhibitor, i. e. a compound which is to be tested whether it is active as an inhibitor to rotamase, is added to the rotamase and tested whether upon the addition and/or influence of the candidate inhibitor the activity of the rotamase is changed relative to the activity without candidate rotamase inhibitor. If the rotamase activity is decreased by the candidate rotamase inhibitor, said candidate rotamase inhibitor is a rotamase inhibitor according to the present invention.

In another aspect of the present invention the compounds according to the present invention may be used in a method for inhibiting a rotamase. In such case a rotamase is provided and a candidate rotamase inhibitor is added thereto whereupon the activity of rotamase is decreased. Optionally, such decrease in rotamase activity is measured. The techniques used theretofore are basically the same as outlined in connection with the use of the compounds according to the present invention as rotamase inhibitors.

In another aspect of the present invention the compounds according to the present invention are used in a method for quantifying the amount of rotamase activity present in a sample and are for

the same purposes used in assays and diagnostic kits for the quantification of rotamases in samples such as blood, lymph, saliva or other tissue samples, bacterial, fungal, plant, yeast, viral or mammalian cell culture. Thus in a preferred embodiment, the sample is assayed using a standard substrate for the appropriate rotamase. A known concentration of a specific inhibitor according to the present invention is added, and allowed to bind to a particular rotamase present. The assay is then rerun, and the loss of activity is correlated to rotamase activity using techniques well known to those skilled in the art. Thus, methods of inhibiting a rotamase are provided, wherein the rotamase inhibitors of the present invention may be added to a sample of rotamase or a sample where it is assumed that a rotamase activity is contained.

The compounds according to the present invention are preferably reversible rotamase inhibitors.

By "reversible" herein is meant that the inhibitor binds non-covalently to the enzyme, and is to be distinguished from irreversible inhibition. See Walsh, Enzymatic Reaction Mechanisms, Freeman & Co., N.Y., 1979. "Reversible" in this context is a term understood by those skilled in the art. Preferably the rotamase inhibitors according to the present invention are competitive inhibitors, that is, they compete with substrate in binding reversibly to the enzyme, with the binding of inhibitor and substrate being mutually exclusive.

In a preferred embodiment of the compounds according to the present invention being active as a rotamase inhibitor, the dissociation constant for inhibition of a rotamase with the inhibitor, generally referred to and characterized by those in the art as K_i, is at most about 100 μM. By the term "binding constant" or "dissociation constant" or grammatical equivalents herein is meant the equilibrium dissociation constant for the reversible association of inhibitor with enzyme. The dissociation constants are defined and determined as described below. The determination of dissociation constants is known in the art. For example, for reversible inhibition reactions such as those of the present invention, the reaction scheme is as follows:

$$E+I \underset{k_2}{\overset{k_1}{\rightleftharpoons}} E^*I \quad \text{(Equation 1)}$$

The enzyme (E) and the inhibitor (I) combine to give an enzyme-inhibitor complex (E*I). This step is assumed to be rapid and reversible, with no chemical changes taking place; the enzyme and the inhibitor are held together by non-covalent forces. In this reaction, k_1 is the second order

rate constant for the formation of the E*I reversible complex. k_2 is the first order rate constant for the dissociation of the reversible E*I complex. In this reaction, $Ki = k_2/k_1$.

The measurement of the equilibrium constant K_i proceeds according to techniques well known in the art. For example, assays generally use synthetic chromogenic or fluorogenic substrates. The respective K_i values may be estimated using the Dixon plot as described by Irwin Segel in Enzyme Kinetics: Behavior and analysis of rapid equilibrium and steady-state enzyme systems, 1975, Wiley-Interscience Publication, John Wiley & Sons, New York, or for competitive binding inhibitors from the following calculation:

$$1-(v_i/v_o)=[I]/[I]+K_i\,(1+([S]/K_m))) \quad \text{(Equation 2)}$$

wherein v_o is the rate of substrate hydrolysis in the absence of inhibitor, and v_i is the rate in the presence of competitive inhibitor.

It is to be understood that dissociation constants are a particularly useful way of quantifying the efficiency of an enzyme with a particular substrate or inhibitor, and are frequently used in the art as such. If an inhibitor exhibits a very low K_i value, it is an efficient inhibitor. Accordingly, the rotamase inhibitors of the present invention have dissociation constants, K_i, of at most about 100 μM. Preferably, the rotamase inhibitors according to the present invention exhibit dissociation constants of at most about 10 μM, more preferably about 1 μM, most preferably of at most about 100 nM.

The rotamase inhibitors of the present invention may be easily screened for their inhibitory effect. The inhibitor is first tested against different classes of rotamases for which the targeting group of the inhibitor was chosen, as outlined above. The activity of rotamases is typically measured by using a protease coupled assay with chromogenic substrates and conformer specific proteases. Basically, upon the conformer specific protease activity the chromogenic substrate is converted into a compound which has an absorption characteristic which is different from the starting chromogenic substrate and may thus be selectively measured. This reaction is accelerated in the presence of the rotamase and decelerated in the presence of rotamase-inhibitors. Alternatively, many rotamases and their corresponding chromogenic substrates are commercially available. Thus, a variety of rotamases are routinely assayed with synthetic chromogenic substrates in the presence and absence of the rotamase inhibitor, to confirm the

inhibitory action of the compound, using techniques well known in the art. The effective inhibitors are then subjected to kinetic analysis to calculate the K_i values, and the dissociation constants determined.

If a compound inhibits at least one rotamase, it is a rotamase inhibitor for the purposes of the present invention. Preferred embodiments of the rotamase inhibitors according to the present invention are compounds and inhibitors, respectively, that exhibit the correct kinetic parameters Ki below 100 μM against the targeted rotamases.

In a further aspect of the present invention any of the compounds used as rotamase inhibitors or as a medicament may be labelled.

By a "labelled rotamase inhibitor" herein is meant a rotamase inhibitor that has at least one element, isotope or chemical compound attached to enable the detection of the rotamase inhibitor or the rotamase inhibitor bound to a rotamase. In general, labels as used herein, fall into three classes: a) isotopic labels, which may be radioactive or heavy isotopes; b) immune labels, which may be antibodies or antigens; and c) colored or fluorescent dyes. The labels may be incorporated into the rotamase inhibitor at any position. Examples of useful labels include ^{14}C, ^{13}C, ^{15}N, ^{3}H, biotin, and fluorescent labels as are well known in the art. Examples for fluorescent labels are fluorescein, 6-FAM, HEX, TET, CY-5, CY-3, CY-7 and Texas Red.

In a further aspect the compounds according to the present invention, particularly those having rotamase inhibitory activity, may be used for removing, identifying and/or inhibiting rotamases, preferably contaminating rotamases, in a sample. Preferably, the sample is a biological sample. Even more preferably such sample is selected from the group comprising blood, lymph, saliva, tissue samples and bacterial, fungal, plant, viral and mammalian cell cultures.

In an embodiment of the present invention the rotamase inhibitors of the present invention are, for example, added to a sample where the catalytic activity by contaminating rotamases is undesirable. Alternatively, the rotamase inhibitors of the present invention may be bound to a chromatographic support, using techniques well known in the art, to form an affinity chromatography column. A sample containing an undesirable rotamase is run through the column to remove the rotamase. Alternatively, the same methods may be used to identify new rotamases. In doing so, a new rotamase contained in a sample may bind to the rotamase inhibitor

bound to the chromatographic support and upon elution, preferably a specific elution, from said chromatographic support, characterized and compared to other rotamase activities with regard to, among others, specificities. The characterization of the rotamase as such is known to the one skilled in the art.

In a further aspect the present invention is related to a pharmaceutical composition comprising a compound according to any of the aspects of the present invention and a pharmaceutically acceptable carrier, diluent or excipient.

In an embodiment the composition comprises a further pharmaceutically active compound, preferably such further pharmaceutically active compound is a chemotherapeutic agent.

In a preferred embodiment of the composition the compound is present as a pharmaceutically acceptable salt or a pharmaceutically active solvate.

In an even more preferred embodiment the pharmaceutically active compound is either alone or in combination with any of the ingredients of the composition present in a multitude of individualized dosages and/or administration forms.

In a further aspect the present invention is related to the use of the compounds according to the present invention as a medicament and for the manufacture of a medicament, respectively.

This use of the compounds according to the present invention is based on the fact that the compounds according to the present invention are inhibitors of rotamases and rotamases in turn have been identified in both procaryotic and eucaryotic cells such as in bacteria, fungi, insect and mammalian cells. In this cellular environment rotamases are known to have an impact on cell proliferation and mitosis, respectively. Because of this, rotamase inhibitors may be used for the treatment of a wide variety of disorders involving cell cycle regulation, both procaryotic and eucaryotic cell cycle regulation. The term "treatment" as used herein comprises both treatment and prevention of a disease. It also comprises follow-up treatment of a disease. Follow-up treatment is realized upon a treatment of a disease using compounds preferably different from the one according to the present invention. For example, after stimulating the growth of a cell, tissue or the like by the application of a respective compound such as, e. g., erythropoietin, it

might be necessary to stop an overshooting reaction of cell proliferation which may be obtained using the compounds according to the present invention.

In a further aspect the present invention is related to the use of the compounds according to the present invention as a medicament and for the manufacture of a medicament, respectively. It is to be understood that any of the compounds according to the present invention can be used for the treatment of or for the manufacture of a medicament for the treatment of any of the diseases disclosed herein, irrespective of the mode of action or the causative agent involved as may be specified herein. Of course, it may particularly be used for any form of such disease where the particular causative agent is involved. Causative agent as used herein also means any agent which is observed in connection with the particular disease described and such agent can be but is not necessarily causative in the sense that is causes the observed diseases or diseased condition.

In an embodiment the medicament is for the treatment or prevention of a disease, whereby the disease involves an undesired cell proliferation.

This use of the compounds according to the present invention is based on the fact that the compounds according to the present invention are suitable to inhibit undesired cell proliferation. Undesired cell proliferation comprises the undesired cell proliferation of procaryotic cells as well as undesired cell proliferation of eucaryotic cells. The term undesired cell proliferation also covers the phenomenon of abnormal cell proliferation, abnormal mitosis and undesired mitosis. Abnormal cell proliferation means any form of cell proliferation which occurs in a manner different from the normal cell proliferation. Normal cell proliferation is a cell proliferation observed under normal circumstances by the majority of cells and organisms, respectively. The same basic definition applies to abnormal mitosis.

More particularly, undesired cell proliferation and undesired mitosis mean a proliferation and a mitosis, respectively, which may be either a normal or an abnormal cell proliferation, however, in any case it is not a cell proliferation or mitosis which is desired. Desired may thus be defined by an individual such as a human being and in particular a physician, and defined within certain boundaries whereby the boundaries as such may reflect the extent of proliferation and mitosis, respectively, observed under usual conditions or in the majority of cells and organisms, respectively, or may be arbitrarily fixed or defined. Cell proliferation as used herein refers

preferably to the proliferation of cells forming the organism to be treated or to which a compound according to the present invention shall be administered which is also referred to herein as the first organism. Cell proliferation as used herein also means the proliferation of cells which are different from the cells forming a first organism or species but are the cells forming a second organism or second species. Typically, the second organism enters in or has a relationship with the first organism. Preferably, the first organism is a human being or an animal or plant, also referred to herein as patient, and the second organism is a parasite and pathogen, respectively, to said first organism. Mitosis as used herein, preferably means the cell division of cells being subject to said cell proliferation whereby even more preferably mitosis is the process of cell division whereby a complete set of chromosomes is distributed to the daughter cells.

Without wishing to be bound by any theory, it seems that the compounds according to the present invention act on cells and thus influence their proliferation and mitosis, respectively, by being inhibitors to some enzymatic activity. Preferably, the inhibition is reversible. This activity is shown by the compounds according to the present invention with regard to bacteria, fungi, insect and mammalian cells.

Because of this, the compounds according to the present invention may be used for the treatment of a wide variety of disorders involving cell cycle regulation, both procaryotic and eucaryotic cell cycle regulation. The term "treatment" as used herein comprises both treatment and prevention of a disease. It also comprises follow-up treatment of a disease. Follow-up treatment is realized upon a treatment of a disease using compounds preferably different from the one according to the present invention. For example, after stimulating the growth of a cell, tissue or the like by the application of a respective compound such as, e. g., erythropoietin, it might be necessary to stop an overshooting reaction of cell proliferation which may be obtained using the compounds according to the present invention.

As used herein, the term "disease" describes any disease, diseased condition or pathological condition. Such disease may also be defined as abnormal condition. Also, in case of a pathogen, disease means a condition where a pathogen or an unwanted organism is present or present in a concentration or compartment where it is undesired and thus subject to reduction in numbers, removal, elimination and/or destruction by using the compounds according to the present invention.

Cell proliferative disorders contemplated for treatment using the compounds according to the present invention and for the methods disclosed herein include disorders characterized by unwanted or undesired, inappropriate or uncontrolled cell growth. Preferably, the disease is selected from the group comprising neurodegenerative diseases, stroke, inflammatory diseases, immune based disorders, infectious diseases, heart diseases, fibrotic disorders, cardiovascular diseases and cell proliferative diseases. Rotamases comprise families of ubiquitous and highly conserved enzymes who have been reported to play important roles in biological processes like protein folding, proteolysis, protein dephosphorylation, peptide transport function, cell cycle regulation, protein synthesis. Furthermore various isomerases have been shown to have regulatory functions as stable or dynamic part of heterooligomeric complexes containing physiologically relevant proteins e.g. hormone receptors, ion channels, kinases, and growth factor receptors.

Preferably, the neurodegenerative disease is selected from the group comprising Alzheimer's disease, Huntington's disease, Parkinson's disease, peripheral neuropathy, progressive supranuclear palsy, corticobasal degeneration, frontotemporal dementia, synucleinopathies, multiple system atrophy, amyotrophic lateral atrophy, prion diseases, and motor neuron diseases.

The compounds according to the present invention are additionally useful in inhibiting cell cycle (mitosis) or cell division in pathogenic organisms and are, therefore, useful for treating infectious diseases.

In a preferred embodiment the infectious is selected from the group comprising fungal, viral, bacterial and parasite infection.

Fungal infections contemplated for treatment using the compounds and methods according to the present invention include systemic fungal infections, dermatophytoses and fungal infections of the genito-urinary tract. Fungal infections, preferably systemic fungal infections, include those caused by *Histoplasma*, *Coccidioides*, *Cryptococcus*, *Blastomyces*, *Paracoccidioides*, *Aspergillus*, *Nocardia*, *Sporothrix*, *Rhizopus*, *Absidia*, *Mucor*, *Hormodendrum*, *Phialophora*, *Rhinosporidium*, and the like. Dermatophyte infections include those caused by *Microsporum*, *Trichophyton*, *Epidermophyton*, *Candida*, *Pityrosporum*, and the like. Fungal disorders of the genito-urinary tract include infections caused by *Candida*, *Cryptococcus*, *Aspergillus*, *Zygomycodoides*, and the like. Infection by such organisms causes a wide variety of disorders

such as ringworm, thrush or candidiasis, San Joaquin fever or Valley fever or coccidiodomycosis, Gilchrist's disease or blastomycosis, aspergillosis, cryptococcosis, histioplasmosis, paracoccidiomycosis, zygomycosis, mycotic keratitis, nail hair and skin disease, Lobo's disease, lobomycosis, chromoblastomycosis, mycetoma, and the like. These infections can be particularly serious, and even fatal, in patients with a depressed immune system such as organ transplant recipients and persons with acquired immunodefficiency syndrome (AIDS). Insofar a patient group which can be treated using the inhibitors according to the present invention are persons with AIDS, particularly those suffering from any of the aforementioned infectious diseases.

In a further embodiment the bacterial infection is selected from the group comprising infections caused by both Gram-positive and Gram-negative bacteria, including infections caused by *Staphylococcus*, *Clostridium*, *Streptococcus*, *Enterococcus*, *Diplococcus*, *Hemophilus*, *Neisseria*, *Erysipelothricosis*, *Listeria*, *Bacillus*, *Salmonella*, *Shigella*, *Escherichia*, *Klebsiella*, *Enterobacter*, *Serratia*, *Proteus*, *Morganella*, *Providencia*, *Yersinia*, *Camphylobacter*, *Mycobacteria*, *Helicobacter*, *Legionalla*, *Nocardia*, and the like.

In a preferred embodiment the bacterial infection causes a wide variety of diseases. Said disorders are selected, among others, from the group comprising pneumonia, diarrhea, dysentery, anthrax, rheumatic fever, toxic shock syndrome, mastoiditis, meningitis, gonorrhea, typhoid fever, brucellis, Lyme disease, gastroenteritis, tuberculosis, cholera, tetanus and bubonic plague.

In another embodiment the disease is a viral infection, more particularly a viral infection caused by a virus selected from the group comprising retrovirus, HIV, Papilloma virus, Polio virus, Epstein-Barr, Herpes virus, Hepatitis virus, Papova virus, Influenza virus, Rabies, JC, encephalitis causing virus, hemorrhagic fever causing virus (such Ebola Virus and Marburg Virus).

In a further embodiment the parasite infection is selected from the group comprising infections caused by *Trypanosoma*, *Leishmania*, *Trichinella*, *Echinococcus*, *Nematodes*, *Classes Cestoda*, *Trematoda*, *Monogenea*, *Toxoplasma*, *Giardia*, *Balantidium*, *Paramecium*, *Plasmodium* or *Entamoeba*.

The disease may further be a cell proliferative disorder which preferably is selected from the group characterized by unwanted, inappropriate or uncontrolled cell growth. Particular examples include cancer, fibrotic disorders, non-neoplastic growths. The neoplastic cell proliferative disorder is preferably selected from the group comprising solid tumors, and hematopoeitic cancers such as lymphoma and leukemia.

More preferably, the solid tumor is selected from the group comprising carcinoma, sarcoma, osteoma, fibrosarcoma, and chondrosarcoma.

More preferably, the cell proliferative disorder is selected from the group comprising breast cancer, prostate cancer, colon cancer, brain cancer, lung cancer, pancreatic cancer, gastric cancer, bladder cancer, kidney cancer and head and neck cancer. Preferably, the lung cancer is non-small lung cancer and small lung cancer.

In case the disease is a non-proliferative cell proliferative disorder, it is preferably selected from the group comprising fibrotic disorder. Preferably, the fibrotic disorder is fibrosis.

The disease may also be a non-neoplastic cell proliferative disorder which is selected from the group comprising prostatic hypertrophy, preferably benign prostatic hypertrophy, endometriosis, psoriasis, tissue repair and wound healing.

Fibrotic disorders which may be treated using the compounds according to the present invention are generally characterized by inappropriate overproliferation of non-cancerous fibroblasts. Examples thereof include fibromyalgia, fibrosis (cystic, hepatic, idopathic pulmonary, pericardial and the like), cardiac fibromas, fibromuscular hyperplasia, restenosis, atherosclerosis, fibromyositis, and the like.

In another embodiment the immune based and/or inflammatory disease is an autoimmune disease or autoimmune disorder. In a further embodiment, the immune based and/or inflammatory disease is selected from the group comprising rheumatoid arthritis, glomerulonephritis, systemic lupus erythematosus associated glomerulonephritis, irritable bowel syndrome, bronchial asthma, multiple sclerosis, pemphigus, pemphigoid, scleroderma, myasthenia gravis, autoimmune haemolytic and thrombocytopenic states, Goodpasture's syndrome, pulmonary hemorrhage, vasculitis, Crohn's disease, and dermatomyositis.

In a further preferred embodiment the immune based and/or inflammatory disease is an inflammatory condition.

In a still further embodiment the immune based and/or inflammatory disease is selected from the group comprising inflammation associated with burns, lung injury, myocardial infarction, coronary thrombosis, vascular occlusion, post-surgical vascular reocclusion, artherosclerosis, traumatic central nervous system injury, ischemic heart disease and ischemia-reperfusion injury, acute respiratory distress syndrome, systemic inflammatory response syndrome, multiple organ dysfunction syndrome, tissue graft rejection and hyperacute rejection of transplanted organs.

In a further embodiment of the various aspects of the present invention the rotamase is human Pin1 and the rotamase involved in the mechanism underlying the various diseases is human Pin1, respectively.

It is also within the present invention that the compounds according to the present invention may be used for the treatment of a patient suffering from a disease or disease condition as defined above. Such treatment comprises the administration of one or several of the compounds according to the present invention or a medicament or pharmaceutical composition described herein.

Toxicity and therapeutic efficacy of a compound can be determined by standard pharmaceutical procedures in cell culture or experimental animals. Cell culture assays and animal studies can be used to determine the LD_{50} (the dose lethal to 50% of a population) and the ED_{50} (the dose therapeutically effective in 50% of a population). The dose ratio between toxic and therapeutic effects is the therapeutic index, which can be expressed as the ratio LD_{50}/ED_{50}. Compounds which exhibit large therapeutic indices are preferred. The data obtained from these cell culture assays and animal studies can be used in formulating a range of dosages suitable for use in humans. The dosage may vary within this range depending upon a variety of factors, e.g., the dosage form employed, the route of administration utilized, the condition of the subject, and the like

For any compound used according to the present invention, the therapeutically effective dose can be estimated initially from cell culture assays by determining an IC_{50} (i.e., the concentration of

the test substance which achieves a half-maximal inhibition of rotamase activity). A dose can then be formulated in animal models to achieve a circulating plasma concentration range that includes the IC_{50} as determined in cell culture. Such information can be used to more accurately determine useful doses in humans. Levels in plasma may be measured, for example by HPLC.

It should be noted that the attending physician would know how to and when to terminate, interrupt, or adjust administration due to toxicity, to organ dysfunction, and the like. Conversely, the attending physician would also know to adjust treatment to higher levels if the clinical response were not adequate (precluding toxicity). The magnitude of an administered dose in the management of the disorder of interest will vary with the severity of the condition to be treated, with the route of administration, and the like. The severity of the condition may, for example, be evaluated, in part, by standard prognostic evaluation methods. Further, the dose and perhaps dose frequency will also vary according to the age, body weight, and response of the individual patient. Typically, the dose will be between about 1-1000 mg/kg of body weight. About 1 mg to about 50 mg will preferably be administered to a child, and between 25 mg and about 1000 mg will preferably be administered to an adult.

A program comparable to that discussed above may be used in veterinary medicine. The exact dose will depend on the disorder to be treated and the amount of rotamases to be inhibited, and will be ascertainable by one skilled in the art using known techniques. For example, as outlined above, some disorders are associated with increased levels of rotamases.

Depending on the specific conditions being treated, such agents may be formulated and administrated systemically or locally. Techniques for formulation and administration may be found in "Remington's Pharmaceutical Sciences", 1990, 18th ed., Mack Publishing Co., Easton, PA. The administration of a compound according to the present invention can be done in a variety of ways, including, but not limited to, orally, subcutaneously, intravenously, intranasally, transdermally, intraperitoneally, intramuscularly, intrapulmonary, vaginally, rectally, or intraocularly, just to name a few. In some instances, for example, in the treatment of wounds and inflammation, the rotamase inhibitors may be directly applied as a solution or spray.

In a further aspect the present invention is related to a medicament or a pharmaceutical composition comprising at least one active compound and at least one pharmaceutically acceptable carrier, excipient or diluent. As used herein, the active compound is a compound

according to the present invention, a pharmaceutically salt or base thereof or a prodrug thereof, if not indicated to the contrary. The active compound may also be a pharmaceutically acceptable derivative of any of the compounds of the present invention. A pharmaceutically acceptable derivative refers to any pharmaceutially acceptable salt or ester of a compound of the present invention, however, is not limited thereto, or any other compound which, upon administration to a patient, is capable of providing, either directly or indirectly, a compound of the present invention, a pharmacologically active metabolite or pharmacologically active residue thereof.

For injection, compounds of the invention may be formulated in aqueous solution, preferably in physiologically compatible buffers such as Hank's solution, Ringer's solution, or physiologically saline buffer. For transmucosal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art.

The use of pharmaceutical acceptable carriers to formulate the compounds according to the present invention into dosages or pharmaceutical compositions suitable for systemic administration is within the scope of the present invention. With proper choice of carrier and suitable manufacturing practice, the compositions of the present invention, in particular those formulated as solutions, may be administered parenterally, such as by intravenous injection. The compounds can be readily formulated using pharmaceutically acceptable carriers well known in the art into dosages suitable for oral administration. Such carriers enable the compounds according to the present invention to be formulated as tablets, pills, capsules, dragees, liquids, gels, syrups, slurries, suspensions and the like, for oral ingestion by a subject to be treated. Suitable pharmaceutical carriers include, but are not limited to, water, salt solutions, alcohols, polyethylene glycols, gelatine, carbohydrates, such as lactose, amylose or starch, magnesium stearate, talc, silicic acid, viscous paraffine, fatty acid esters, hydroxymethylcellulose, polyvinylpyrolidone and the like.

Compounds according to the present invention or medicaments comprising them intended to be administered intracellularly may be administered using techniques well known to those of ordinary skill in the art. For example, such agents may be encapsulated into liposomes, then administered as described above. Liposomes are spherical lipid bilayers with aqueous interiors. All molecules present in an aqueous solution at the time of liposome formation are incorporated into the aqueous interior. The liposomal contents are both protected from the external microenvironment and, because liposomes fuse with cell membranes, are efficiently delivered

into the cell cytoplasm. Delivery systems involving liposomes are discussed in International Patent Publication No. WO 91/19501, as well as U.S. Patent No. 4,880,635 to Janoff et al. The publications and patents provide useful descriptions of techniques for liposome drug delivery and are incorporated by reference herein in their entirety.

Pharmaceutical compositions comprising a compound according to the present invention for parenteral administration include aqueous solutions of the active compound(s) in water-soluble form. Additionally, suspensions of the active compounds may be prepared as appropriate oily injection suspensions. Suitable lipophilic solvents or vehicles include fatty oils such as sesame oil, or synthetic fatty acid esters, such as ethyl oleate or triglycerides, or liposomes. Aqueous injections suspensions may contain compounds which increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, dextran, or the like. Optionally, the suspension may also contain suitable stabilizers or agents which increase the solubility of the compounds to allow for the preparation of highly concentrated solutions.

Pharmaceutical compositions comprising a compound according to the present invention for oral use can be obtained by combining the active compound(s) with solid excipient, optionally grinding the resulting mixture, and processing the mixture of granules, after adding suitable auxiliaries, if desired, to obtain tablets or dragee cores.

Suitable excipients are, in particular, fillers such as sugars, including lactose, sucrose, mannitol, sorbitol, and the like; cellulose preparations, such as, for example, maize starch, wheat starch, rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl cellulose, sodium carboxymethyl cellulose, polyvinylpyrrolidone (PVP) and the like, as well as mixtures of any two or more thereof. If desired, disintegrating agents may be added, such as cross-linked polyvinyl pyrrolidone, agar, alginic acid or a salt thereof such as sodium alginate, and the like.

Dragee cores as a pharmaceutical composition comprising a compound according to the present invention are provided with suitable coatings. For this purpose, concentrated sugar solutions may be used, which may optionally contain gum arabic, talc, polyvinyl pyrrolidone, carbopol gel, polyethylene glycol, titanium dioxide, lacquer solutions, suitable organic solvents or solvent mixtures, and the like. Dyestuffs or pigments may be added to the tablets or dragee coatings for identification or to characterize different combinations of active compound doses.

Pharmaceutical preparations comprising a compound according to the present invention which can be used orally include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a plasticizer, such as glycerol or sorbitol. The push-fit capsules can contain the active ingredients in admixture with filler such as lactose, binders such as starches and/or lubricants such as talc or magnesium stearate and, optionally, stabilizers. In soft capsules, the active compounds may be dissolved or suspended in suitable liquids, such as fatty oils, liquid paraffin, or liquid polyethylene glycols. In addition, stabilizers may be added.

A "patient" for the purposes of the present invention, i. e. to whom a compound according to the present invention or a pharmaceutical composition according to the present invention is administered, includes both humans and other animals and organisms. Thus the compounds, pharmaceutical compositions and methods are applicable to or in connection with both human therapy and veterinary applications. For example, the veterinary applications include, but are not limited to, canine, bovine, feline, porcine, caprine, equine, and ovine animals, as well as other domesticated animals including reptiles, such as iguanas, turtles and snakes, birds such as finches and members of the parrot family, lagomorphs such as rabbits, rodents such as rats, mice, guinea pigs and hamsters, amphibians, fish, and arthropods. Valuable non-domesticated animals, such as zoo animals, may also be treated. In the preferred embodiment the patient is a mammal, and in the most preferred embodiment the patient is human.

The pharmaceutical composition according to the present invention comprises at least one compound according to the present invention, preferably a rotamase inhibitor according to the present application, in a form suitable for administration to a patient. Preferably, a compound according to the present application is in a water soluble form, such as being present as a pharmaceutically acceptable salt, which is meant to include both acid and base addition salts. "Pharmaceutically acceptable acid addition salt" refers to those salts that retain the biological effectiveness of the free bases and that are not biologically or otherwise undesirable, formed with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid and the like, and organic acids such as acetic acid, propionic acid, glycolic acid, pyruvic acid, oxalic acid, maleic acid, malonic acid, succinic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, salicylic acid and the like. "Pharmaceutically acceptable base addition salts" include those derived from inorganic bases such as sodium, potassium, lithium,

ammonium, calcium, magnesium, iron, zinc, copper, manganese, aluminum salts and the like. Particularly preferred are the ammonium, potassium, sodium, calcium, and magnesium salts. Salts derived from pharmaceutically acceptable organic non-toxic bases include salts of primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines and basic ion exchange resins, such as isopropylamine, trimethylamine, diethylamine, triethylamine, tripropylamine, and ethanolamine. The pharmaceutical compositions according to the present invention may also include one or more of the following: carrier proteins such as serum albumin; buffers; fillers such as microcrystalline cellulose, lactose, corn and other starches; binding agents; sweeteners and other flavoring agents; coloring agents; and polyethylene glycol. Additives are well known in the art, and are used in a variety of formulations.

The compounds according to the present invention are, in a further embodiment, administered to a subject either alone or in a pharmaceutical composition where the compound(s) is mixed with suitable carriers or excipient(s). In treating a subject, a therapeutically effective dose of compound (i.e. active ingredient) is administered. A therapeutically effective dose refers to that amount of the active ingredient that produces amelioration of symptoms or a prolongation of survival of a subject which can be determined by the one skilled in the art doing routine testing.

On the other hand, the compounds according to the present invention which have a rotamase inhibitory activity may as such or contained in a pharmaceutical composition according to the present invention be used in drug potentiation applications.

For example, therapeutic agents such as antibiotics or antitumor drugs can be inactivated through the catalytic action of endogenous rotamases, thus rendering the administered drug less effective or inactive. Accordingly, the rotamase inhibitors of the invention may be administered to a patient in conjunction with a therapeutic agent in order to potentiate or increase the activity of the drug. This co-administration may be by simultaneous administration, such as a mixture of the rotamase inhibitor and the drug, or by separate simultaneous or sequential administration.

According to the present invention the compounds disclosed herein, referred to as compounds according to the present invention, may be used as a medicament or for the manufacture of medicament or in a method of treatment of a patient in need thereof. Insofar any of these

compounds constitute a pharmaceutical compound. The use of this kind of compound also comprises the use of pharmaceutically acceptable derivatives of such compounds.

In addition, the compounds according to the present invention may be transformed upon application to an organism such as a patient, into the pharmaceutically active compound. Insofar the compounds according to the present invention may be prodrugs which, however, are nevertheless used for the manufacture of the medicaments as disclosed herein given the fact that at least in the organism they are changed in a form which allows the desired pharmaceutical effect.

It is to be understood that any of the pharmaceutical compositions according to the present invention may be used for any of the diseases or conditions described herein.

The pharmaceutical compositions according to the present invention may be manufactured in a manner that itself is known, e.g., by means of conventional mixing, dissolving, granulating, dragee-mixing, levigating, emulsifying, encapsulating, entrapping, lyophilizing, processes, or the like.

In a further aspect of the present invention the compounds of the present invention may be used as insecticides as they may prevent cell cycle mitosis in insect cells and thus can be used to control the growth and proliferation of a variety of insect pests. This aspect of the present invention has important applications in agriculture, such as in the field, in the storage of agricultural products and the like. Additionally, the compounds according to the present invention are useful for controlling insect populations, preferably in places inhabited by men, such as homes, offices and the like.

Any of the compounds according to the present invention containing one or more asymmetric carbon atoms may occur as racemates and racemic mixtures, single enantiomers, diastereomeric mixtures and individual diastereomers. All such isomeric forms of these compounds are expressly included in the present invention. Each stereogenic carbon may be in the R or S configuration, or a combination of configurations.

It shall be understood by one of ordinary skill in the art that all compounds of the invention are those which are chemically stable. This applies to any of the various uses of the compounds according to the present invention disclosed herein.

In determining the suitability of any of the compounds according to the present applications for the various uses, besides the particular profile to be met by such a compound, also it has to be checked whether it is stable to proteolytic degradation. The resistance of the compound used as rotamase inhibitor or pharmaceutical may be tested against a variety of non-commercially available rotamases *in vitro* to determine its proteolytic stability. Promising candidates may then be routinely screened in animal models, for example using labelled inhibitors, to determine the *in vivo* stability and efficacy. In any of the aforementioned uses the compound may be present in a crude or purified form. Methods for purifying the compounds according to the present invention are known to the one skilled in the art.

The invention is now further illustrated by reference to the following figure and examples from which further advantages, features and embodiments may be taken. It is understood that these examples are given for purpose of illustration only and not for purpose of limitation. All references cited herein are incorporated by reference.

Figs. 1 to 6b show various methods for the synthesis of the compounds according to the present invention which will be explained in more detail in the following examples.

EXAMPLE 1

General synthetic methods

Compounds of the invention may in principle be synthesized by methods described below. In addition, further methods for the synthesis of the known compounds used according to the present invention are described, for example, in WO 01/19816, WO 01/30772, US patent application 2001/0046207, US 4,927,809; WO 00/55126, WO 99/56765, WO 01/09110, WO 01/47886, WO 00/49008, WO 99/24460, WO 00/51998, WO 00/48992 and WO 01/49288. Standard peptide coupling, protection and deprotection reactions (M. Bodansky, The Practice of Peptide Synthesis, Springer-Verlag, 1984) are employed in these syntheses.

As used herein, the following abbreviations are used:

Ar is argon;
Boc is tertiary butoxy carbamoyl;
Bth is benzo[b]thiophen-2-yl;
t-Bu is tertiary butyl;
DCM is dichloromethane;
DIC is diisopropyl carbodiimide;
DIPEA is *N,N*-diisopropylethylamine;
DMF is *N,N*-dimethylformamide;
DMSO is *N,N*-dimethylsulfoxide;
eq is equivalent;
Et_3N is triethylamine;
EtOAc is ethyl acetate;
HBTU is 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate;
HPLC is high performance liquid chromatography;
h is hour;
MeOH is methanol;
$MgSO_4$ is magnesium sulfate;
NaCl is sodium chloride;
$NaHCO_3$ is sodium hydrogencarbonate;
Nal is naphthalene-2-yl;
PyBrOP is benzotriazole-1-yl-oxy-tris-pyrrolidino-phosphonium hexafluorophosphate;
TFA is trifluoroacetic acid

According to scheme 1 depicted in Fig. 1 suitable protected amino acid derivatives 1 bearing R_5, R_6, R_7 and 4 bearing R_5, R_6, R_7, R_8, R_9 are transformed to the corresponding primary amides 2 and 5 using ammonia or ammonium chloride under standard coupling conditions typically used in peptide synthesis. Suitable protecting groups (R_5) for the amino functions are the t-butoxycarbonyl (Boc), 9-fluorenylmethoxycarbonyl (Fmoc), and other groups. Examples of standard coupling conditions would be reacting the protected amino acid derivatives 1 and 4 in the presence of a coupling reagent such as benzotriazol-1-yloxytrispyrrolidinophosphonium hexafluorophosphate (PyBOP®), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI), *O*-benzotriazol-1-yl-*N,N,N',N'*-tetramethyluronium hexafluorophosphate (HBTU), 1,3-

dicyclohexylcarbodiimide (DCC), or the like, in a suitable solvent (*N*-methylpyrrolidinone, DMF, DCM, or the like). Additionally an appropriate catalyst (e.g., 1-hydroxybenzotriazole (HOBT), 1-hydroxy-7-azabenzotriazole (HOAt), or the like) and non-nucleophilic bases (e.g., *N*-methylmorpholine, triethylamine, *N,N*-diisopropylethylamine or the like, or any suitable combination thereof) may be added. The resulting amides are converted to the corresponding nitriles 3 and 6 by dehydration. Suitable dehydratation conditions can be cyanuric chloride in DMF, trifluoroacetic anhydride in DCM in the presence of pyridine (N. D. Hone, L. J: Payne, C. M. Tice, *Tetrahedron Lett.*, (2001) **42**, 1115-1118), benzoylsulfonyl chloride in pyridine (T. T. Van, E. Kojro, Z. Grzonka, *Tetrahedron* (1977) **33**, 2299).

According to scheme 2 depicted in Fig. 2 suitable protected building block derivatives 8 bearing R_5, R_6, R_7 and 10 bearing R_5, R_6, R_7, R_8, R_9 are reacted with activated amino acid derivatives 7 bearing R_2, R_3, R_4 under standard coupling conditions used in peptide synthesis.the resulting derivatives 9 and 11 are obtained after deprotection of the amine.

According to scheme 3a depicted in Fig. 3a a suitable protected amines 9 bearing R_2, R_3, R_4, R_5, R_6, R_7 are allowed to react with different reagents. They can be reacted with acids, acyl chlorides or anhydrides to provide 9a. Acids can be condensed by standard peptide coupling conditions such as PyBrOP, DIPEA, 1-hydroxybenzotriazole-6-sulfonamidomethyl polystyrene in dry DMF (I. E. Pop, *J. Org. Chem.* (1997) **62**, 2594). Acyl chlorides or anhydrides can be reacted in dry DCM in the presence of a non nucleophilic base like DIPEA followed by sequestering any remaining acyl chlorides or anhydride by a polymer-supported quenching reagent like tris-(2-aminoethyl)-amine polystyrene (R. J. Booth, J. C. Hodges, *J. Am. Chem. Soc.* (1997) **119**, 4882; M. W. Creswell, G. L. Bolton, J. C. Hodges, M. Meppen, *Tetrahedron* (1998) **54**, 3983). Sulfonamide derivatives 9b are obtained after reaction with different sulfonyl chlorides in dry DCM in the presence of a non nucleophilic base like DIPEA followed by sequestering any remaining sulfonyl chloride by a polymer-supported quenching reagent like tris-(2-aminoethyl)-amine polystyrene (R. J. Booth, J. C. Hodges, *J. Am. Chem. Soc.* (1997) **119**, 4882). Carbamates 9c (R. J. Booth, J. C. Hodges, *J. Am. Chem. Soc.* (1997) **119**, 4882) are obtained by reacting chloroformates in dry DCM in the presence of a non nucleophilic base like DIPEA, followed by sequestering any remaining chloroformate by a polymer-supported quenching reagent like tris-(2-aminoethyl)-amine polystyrene. Thioureas 9d and ureas 9e were obtained after reaction with thio-isocyanates or isocyanates in DCM in the presence of a non nucleophilic base like DIPEA, followed by sequestering any remaining thio-isocyanate or isocyanate by a polymer-supported

quenching reagent like tris-(2-aminoethyl)-amine polystyrene (R. J. Booth, J. C. Hodges, *J. Am. Chem. Soc.* (1997) **119**, 4882).

According to scheme 3b depicted in Fig. 3b suitable protected amines 11 bearing R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9 is allowed to react with different reagents as described for scheme 3 a.

According to scheme 4 depicted in Fig. 4 suitable protected dipeptides 1 bearing R_5, R_6, R_7 or 7 R_5, R_6, R_7, R_8, R_9 are coupled with a resin like Rink amide PEGA resin in the presence of a coupling reagent such as benzotriazol-1-yloxytrispyrrolidinophosphonium hexafluorophosphate (PyBOP®), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI), *O*-benzotriazol-1-yl-*N,N,N',N'*-tetramethyluronium hexafluorophosphate (HBTU), 1,3-dicyclohexylcarbodiimide (DCC), or the like, in a suitable solvent (*N*-methylpyrrolidinone, DMF, DCM, or the like). Additionally an appropriate catalyst (e.g., 1-hydroxybenzotriazole (HOBT), 1-hydroxy-7-azabenzotriazole (HOAt), or the like) and non-nucleophilic bases (e.g., *N*-methylmorpholine, triethylamine, *N,N*-diisopropylethylamine or the like, or any suitable combination thereof) may be added. An example of a suitable protecting group for the amine function is the 9-fluorenylmethoxycarbonyl (Fmoc) group. This is followed by deprotection to give the free amine. An example of a suitable deprotection is piperidine in DMF. A suitable protected building block bearing R_2, R_3, R_4 is then coupled in the same conditions ad described before. Desired compounds 14 and 17 are obtained after deprotection of the amine function.

According to scheme 5a depicted in Fig. 5a suitable protected immobilized amines 14 bearing R_2, R_3, R_4, R_5, R_6, R_7 are allowed to react with different reagents. They can be reacted with acids, acyl chlorides or anhydrides to provide the corresponding amides 14a. An example of standard coupling conditions with acide would be to combine with HBTU and diisopropylethylamine in anhydrous DMF. Acyl chloride or anhydride would be reacted in dry DCM in the presence of a non nucleophilic base like DIPEA (B. Raju, T. P. Kogan, *Tetrahedron Lett.* (1997) 38, 4965). Sulfonamide derivatives 14b are obtained after reaction with differents sulfonyl chlorides in dry DCM in the presence of DMAP (C. Gennari, B. Salom, D. Potenza, A. Williams, *Angew. Chem., Int. Ed. Engl.* (1994) 33 2067). Carbamates 14c are obtained by reacting chloroformates in dry DCM in the presence of a non nucleophilic base like DIPEA (T. Fukuyama, L. Li, A. A. Laird, R. K. Frank, *J. Am. Chem. Soc.* (1987) **109**, 1587). Thioureas 14d and ureas 14e were obtained after reaction with thio-isocyanates or isocyanates in DCM with or

without a non nucleophilic base like DIPEA (P. C. Kearney, M. Fernandez, J. A. Flygare, *J. Am. Chem. Soc.* (1998) 63, 196).

According to scheme 5b depicted in Fig. 5b suitable protected immobilized amines 17 bearing R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9 are allowed to react with different reagents as described for scheme 5 a.

According to scheme 6a depicted in Fig. 6a suitable immobilized derivatives 14 a-e bearing R_1, R_2, R_3, R_4, R_5, R_6, R_7 are cleaved from the resin to give the amides 18 a-e that are converted to the corresponding nitriles 19 a-e by dehydration. An example of a suitable cleavage is TFA in DCM. The nitriles 19 a-e are also obtained directly from the immobilized derivatives 14 a-e using trifluoroacetic anhydride for the dehydration.

According to scheme 6b depicted in Fig. 6b suitable immobilized derivatives 17 a-e bearing R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9 are reacted to give the corresponding nitriles 21 a-e as described for scheme 6 a.

Method A: Coupling of acyl chlorides with derivatized amines in solution.
Amine salt (1 eq) was dissolved in a mixture of 10% dry DMSO in anhydrous DCM, acyl chloride (1.5 eq) and diisopropylethylamine (2 eq) were added under Ar, and stirred for 2 h at room temperature. Tris-(2-aminoethyl)-amine polystyrene (6 eq relative to excess acyl chloride) and (polystyrylmethyl)trimethylammonium bicarbonate (4 eq relative to expected amine salt) were added to the reaction mixture and agitated for 18 h at room temperature. The supernatant was separated from the resin by filtration and the polymeric beads were washed with DCM and a mixture of DCM/MeOH (1/1) (three times). After evaporation of the solvent, the residue was dissolved/suspended in water and lyophilized to give the crude product.

Method B: Coupling of anhydrides with derivatized amines in solution.
Amine salt (1 eq) was dissolved in a mixture of 10% dry DMSO in anhydrous DCM, anhydride (1.5 eq) and diisopropylethylamine (2 eq) were added under Ar, and stirred for 18 h at room temperature. Tris-(2-aminoethyl)-amine polystyrene (6 eq relative to excess anhydride) and (polystyrylmethyl)trimethylammonium bicarbonate (4 eq relative to expected amine salt) were added to the reaction mixture and agitated for 18 h at room temperature. The supernatant was

separated from the resin by filtration and the polymeric beads were washed with DCM and a mixture of DCM/MeOH (1/1) (three times). After evaporation of the solvent, the residue was dissolved/suspended in water and lyophilized to give the crude product.

Method C: Coupling of chloroformates with derivatized amines in solution.

Amine salt (1 eq) was dissolved in a mixture of 10% dry DMSO in anhydrous DCM, chloroformate (1.5 eq) and diisopropylethylamine (2 eq) were added under Ar, and stirred for 18 h at room temperature. Tris-(2-aminoethyl)-amine polystyrene (6 eq relative to excess anhydride) and (polystyrylmethyl)trimethylammonium bicarbonate (4 eq relative to expected amine salt) were added to the reaction mixture and agitated for 18 h at room temperature. The supernatant was separated from the resin by filtration and the polymeric beads were washed with DCM and a mixture of DCM/MeOH (1/1) (three times). After evaporation of the solvent, the residue was dissolved/suspended in water and lyophilized to give the crude product.

Method D: Coupling of acids with derivatized amines in solution.

Method D1: Coupling using 1-hydroxybenzotriazole-6-sulfonamidomethyl polystyrene

To a solution of PyBrOP (2 eq), acid (2 eq) and diisopropylethylamine (4 eq) in anhydrous DMF was added 1-hydroxybenzotriazole-6-sulfonamidomethyl polystyrene (2 eq). The mixture was reacted at room temperature for 5 h. After the first activation step the resin was washed with DMF (three times). The second activation step was performed under the same conditions as the first one, and the resin was washed with DMF (five times).

The amine salt (1 eq) was added to a suspension of the resin in anhydrous DCM and diisopropylethylamine (2 eq). The polymer-bound activated ester was reacted with this mixture at room temperature. After 20 h, the supernatant was separated from the resin by filtration. The polymeric beads were washed with DCM and a mixture of DCM/MeOH (1/1) (three times), the solvent was removed under vacuum. The residue was dissolved/suspended in water, and lyophilized to give the crude product.

Method D2: Coupling using *N*-cyclohexylcarbodiimide, *N'*-methyl polystyrene

Amine salt (1 eq) and acid (1.5 eq) in a mixture of 10% dry DMSO in anhydrous DCM were stirred under Ar. After 10 min *N*-cyclohexylcarbodiimide, *N'*-methyl polystyrene (2 eq) was added. The reaction was stirred overnight at room temperature. The supernatant was separated from the resin by filtration. The polymeric beads were washed with DCM and a mixture of

DCM/MeOH (1/1) (three times), the solvent was removed under vacuum. The residue was dissolved/suspended in water and lyophilized to give the crude product.

Method D3: Coupling using standard conditions for peptides

To a solution of amine salt (1 eq) in anhydrous DMF was added the acid (1 eq), HBTU (1 eq) and Et_3N (2 eq). The reaction mixture was stirred overnight and then diluted with EtOAc. The organic phase was washed with saturated aqueous solution of $NaHCO_3$ and saturated aqueous solution of NaCl, dried over $MgSO_4$, filtered and evaporated. The residue was purified by flash-chromatography.

Method E: Coupling of sulfonyl chlorides with derivatized amines in solution.

Amine salt (1 eq) was dissolved in a mixture of 10% dry DMSO in anhydrous DCM, sulfonyl chloride (1.5 eq) and diisopropylethylamine (4 eq) were added under Ar, and stirred 2 h at room temperature. Tris-(2-aminoethyl)-amine polystyrene (3 eq relative to excess sulfonyl chloride) and (polystyrylmethyl)trimethylammonium bicarbonate (4 eq relative to expected amine salt) were added to the reaction mixture and agitated for 18 h at room temperature. The supernatant was separated from the resin by filtration, the polymeric beads were washed with DCM and a mixture of DCM/MeOH (1/1) (three times). After evaporation of the solvent, the residue was dissolved/suspended in water and lyophilized to give the crude product.

Method F: Coupling of isocyanates with derivatized amines in solution.

Amine salt (1 eq) was dissolved in a mixture of 10% dry DMSO in anhydrous DCM, isocyanate (1.5 eq) and diisopropylethylamine (2 eq) were added under Ar, and stirred for 2 h at room temperature. Tris-(2-aminoethyl)-amine polystyrene (3 eq relative to excess isocyanate) and (polystyrylmethyl)trimethylammonium bicarbonate (4 eq relative to expected amine salt) were added to the reaction mixture and agitated for 18 h at room temperature. The supernatant was separated from the resin by filtration, the polymeric beads were washed with DCM and a mixture of DCM/MeOH (1/1) (three times). After evaporation of the solvent, the residue was dissolved/suspended in water, and lyophilized to give the crude product.

Method G: Coupling of thio-isocyanates with derivatized amines in solution.

Amine salt (1 eq) was dissolved in a mixture of 10% dry DMSO in anhydrous DCM, thio-isocyanate (1.5 eq) and diisopropylethylamine (2 eq) were added under Ar, and stirred for 5 h at room temperature. Tris-(2-aminoethyl)-amine polystyrene (6 eq relative to excess thio-

isocyanate) and (polystyrylmethyl)trimethylammonium bicarbonate (4 eq relative to expected amine salt) were added to the reaction mixture and agitated for 18 h at room temperature The supernatant was separated from the resin by filtration, the polymeric beads were washed with DCM and a mixture of DCM/MeOH (1/1) (three times). After evaporation of the solvent, the residue was dissolved/suspended in water, and lyophilized to give the crude product.

Method H: Coupling of acyl chlorides with derivatized amines on solid-phase.

The immobilized amine (1 eq) was swollen in anhydrous DCM, acyl chloride (5 eq) and diisopropylethylamine (5 eq) were added, the mixture was shaken 18 h at room temperature. The resin was filtered off and washed successively with DMF, methanol, and dichloromethane and dried. A solution of 50% trifluoroacetic acid in dichloromethane was added to the resin. The mixture was shaken 30 min at room temperature. After filtration, the resin was washed with a solution of 50% trifluoroacetic acid in dichloromethane. After evaporation of the solvent, the residue was dissolved/suspended in water, and lyophilized to give the crude product.

Method I: Coupling of anhydrides with derivatized amines on solid-phase.

The immobilized amine (1 eq) was swollen in anhydrous DCM, anhydride (5 eq) and diisopropylethylamine (5 eq) were added, the mixture was shaken 18 h at room temperature. The resin was filtered off and washed successively with DMF, methanol, and dichloromethane and dried. A solution of 50% trifluoroacetic acid in dichloromethane was added to the resin. The mixture was shaken 30 min at room temperature. After filtration, the resin was washed with a solution of 50% trifluoroacetic acid in dichloromethane. After evaporation of the solvent, the residue was dissolved/suspended in water, and lyophilized to give the crude products.

Method J: Coupling of chloroformates with derivatized amines on solid-phase.

The immobilized amine (1 eq) was swollen in anhydrous DCM, chloroformate (5 eq) and diisopropylethylamine (5 eq) were added, the mixture was shaken 18 h at room temperature. The resin was filtered off and washed successively with DMF, methanol, and dichloromethane and dried. A solution of 50% trifluoroacetic acid in dichloromethane was added to the resin. The mixture was shaken 30 min at room temperature. After filtration, the resin was washed with a solution of 50% trifluoroacetic acid in dichloromethane. After evaporation of the solvent, the residue was dissolved/suspended in water, and lyophilized to give the crude products.

Method K: Coupling of acids with derivatized amines on solid-phase.

Acid (5 eq) was preactivated with HBTU (5 eq) and diisopropylethylamine (5 eq) in anhydrous DMF for 5 min, and added to the immobilized amine (1 eq). The mixture was shaken 18 h at room temperature. The resin was filtered off and washed successively with DMF, methanol, and dichloromethane and dried. A solution of 50% trifluoroacetic acid in dichloromethane was added to the resin. The mixture was shaken 30 min at room temperature. After filtration, the resin was washed with a solution of 50% trifluoroacetic acid in dichloromethane. After evaporation of the solvent, the residue was dissolved/suspended in water, and lyophilized to give the crude product.

Method L: Coupling of sulfonyl chlorides with derivatized amines on solid-phase.

The immobilized amine (1 eq) was swollen in anhydrous DCM, sulfonyl chloride (5 eq) and DMAP (5 eq) were added, the mixture was shaken 18 h at room temperature. The resin was filtered off and washed successively with DMF, methanol, and dichloromethane and dried. A solution of 50% trifluoroacetic acid in dichloromethane was added to the resin. The mixture was shaken 30 min at room temperature. After filtration, the resin was washed with a solution of 50% trifluoroacetic acid in dichloromethane. After evaporation of the solvent, the residue was dissolved/suspended in water, and lyophilized to give the crude product.

Method M: Coupling of isocyanates with derivatized amines on solid-phase.

The immobilized amine (1 eq) was swollen in anhydrous DCM, isocyanate (5 eq) was added and the mixture was shaken 18 h at room temperature. The resin was filtered off and washed successively with DMF, methanol, and dichloromethane and dried. A solution of 50% trifluoroacetic acid in dichloromethane was added to the resin. The mixture was shaken 30 min at room temperature. After filtration, the resin was washed with a solution of 50% trifluoroacetic acid in dichloromethane. After evaporation of the solvent, the residue was dissolved/suspended in water, and lyophilized to give the crude product.

Method N: Coupling of thio-isocyanates with derivatized amines on solid-phase.

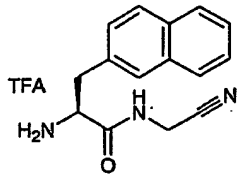
The immobilized amine (1 eq) was swollen in anhydrous DCM, thio-isocyanate (5 eq) was added and the mixture was shaken 18 h at room temperature. The resin was filtered off and washed successively with DMF, methanol, and dichloromethane and dried. A solution of 50% trifluoroacetic acid in dichloromethane was added to the resin. The mixture was shaken 30 min at room temperature. After filtration, the resin was washed with a solution of 50% trifluoroacetic

acid in dichloromethane. After evaporation of the solvent, the residue was dissolved/suspended in water, and lyophilized to give the crude product.

Compounds were purified by HPLC.

EXAMPLE 2

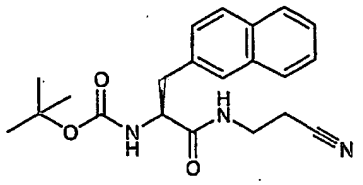
2-Amino-3-naphthalen-2-yl-propionic acid cyanomethyl-amide trifluoroacetate



To a solution of 3-aminoacetonitrile hydrogensulfate (1.61 g, 1.25 eq) in anhydrous DMF (36 mL) was added Boc-β-Nal-OH (3 g, 1 eq), HBTU (3.62 g, 1 eq) and Et_3N (4 mL, 3.8 eq). The reaction mixture was stirred overnight and then diluted with EtOAc. The organic phase was washed with saturated aqueous solutions of $NaHCO_3$ and NaCl, dried over $MgSO_4$, filtered and evaporated. The residue was purified by flash-chromatography hexane/ethyl acetate 3/2 to give [1-(cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid tert-butyl ester. The ester was dissolved in a solution of 50% TFA in DCM (15 mL), stirred at room temperature for 15 min and then evaporated with toluene. The residue was purified by HPLC to give 2-amino-3-naphthalen-2-yl-propionic acid cyanomethyl-amide trifluoroacetate (2.5 g, 70%).

EXAMPLE 3

[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid tert-butyl ester



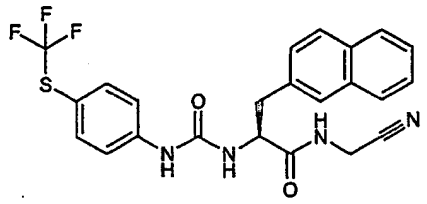
To a solution of 3-aminopropionitrile (146 µL, 1.25 eq) in anhydrous DMF (4.3 mL) was added Boc-β-Nal-OH (500 mg, 1 eq), HBTU (601.3 mg, 1 eq) and Et_3N (331.5 µL, 1.5 eq). The reaction mixture was stirred overnight and then diluted with EtOAc. The organic phase was washed with saturated aqueous solutions of $NaHCO_3$ and NaCl, dried over $MgSO_4$, filtered and evaporated. The residue was purified by flash-chromatography hexane/ethyl acetate 3/2 to give

[1-(cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid tert-butyl ester (559 mg, 96%).

NMR-^{1}H (DMSO-d_6) δ = 1.24 (s, 9 H), 2.61 (m, 2 H), 2.93 (dd, 1 H, J = 10.3, J = 13.7 Hz, 1 H), 3.13 (dd, 1 H, J = 4.3, J = 13.7 Hz, 1 H), 3.37 (m, 2 H), 4.24 (m, 1 H), 6.99 (d, J = 8.6 Hz, 1 H), 7.43-7.50 (m, 3 H), 7.73-7.87 (m, 3 H), 8.33 (m, 1 H); MS: *m/z*: 367.8 [M^+].

EXAMPLE 4

3-Naphthalen-2-yl-2-[3-(4-trifluoromethylsulfanyl-phenyl)-ureido]-propionic acid cyanomethyl-amide

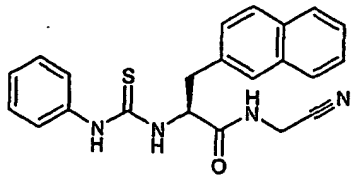


Amine salt (prepared as described in example 1) (10 mg) was dissolved in a mixture of 10% dry DMSO (100 µL) in anhydrous DCM (1 mL), 4-(trifluoromethylthio)-phenyl isocyanate (6.98 µL) and diisopropylethylamine (10 µL) were added under Ar, and stirred for 2 h at room temperature. Tris-(2-aminoethyl)-amine polystyrene (10 mg) and (polystyrylmethyl) trimethylammonium bicarbonate (10 mg) were added to the reaction mixture and agitated for 18 h at room temperature The supernatant was separated from the resin by filtration, the polymeric beads were washed with DCM and a mixture of DCM/MeOH (1/1) (three times). After evaporation of the solvent, the residue was was purified by HPLC to give 3-naphthalen-2-yl-2-[3-(4-trifluoromethylsulfanyl-phenyl)-ureido]-propionic acid cyanomethyl-amide (13.4 mg, 98%).

NMR-^{1}H (DMSO-d_6) δ = 3.06 (dd, 1 H, J = 7.7, J = 13.7 Hz), 3.19 (dd, 1 H, J = 5.8, J = 13.7 Hz), 4.18 (m, 2 H), 4.60 (m, 1 H), 7.38 (m, 1 H), 7.43-7.52 (m, 4 H), 7.63 (m, 2 H), 7.70 (s, 1 H), 7.82-7.88 (m, 3 H), 8.90 (m, 1 H); MS: *m/z*: 472.9 [M^+].

EXAMPLE 5

3-Naphthalen-2-yl-2-(3-phenyl-thioureido)-propionic acid cyanomethyl-amide

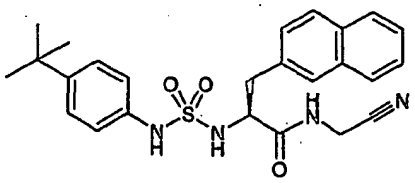


Amine salt (prepared as described in example 1) (10 mg) was dissolved in a mixture of 10% dry DMSO (100 µL) in anhydrous DCM (1 mL), phenyl isothiocyanate (5.20 µL) and diisopropylethylamine (10 µL) were added under Ar, and stirred for 5 h at room temperature. Tris-(2-aminoethyl)-amine polystyrene (10 mg) and (polystyrylmethyl)trimethylammonium bicarbonate (10 mg) were added to the reaction mixture and agitated for 18 h at room temperature. The supernatant was separated from the resin by filtration, the polymeric beads were washed with DCM and a mixture of DCM/MeOH (1/1) (three times). After evaporation of the solvent, the residue was purified by HPLC to give 3-naphthalen-2-yl-2-(3-phenyl-thioureido)-propionic acid cyanomethyl-amide (10.5 mg, 93%).

NMR-^{1}H (DMSO-d_6) δ = 3.21 (m, 1 H), 3.29 (m, 1 H), 4.18 (m, 2 H), 5.26 (m, 1 H), 7.09 (m, 1 H), 7.26 (m, 2 H), 7.36 (m, 3 H), 7.49 (m, 2 H), 7.69 (s, 1 H), 7.82-7.90 (m, 3 H), 8.92 (m, 1 H), 9.82 (s, 1 H); MS: *m/z*: 388.9 [M^+].

EXAMPLE 6

3-Naphthalen-2-yl-2-(4-tert-butyl-benzenesulfonylamino)-propionic acid cyanomethyl-amide



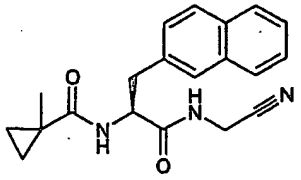
Amine salt (prepared as described in example 1) (10 mg) was dissolved in a mixture of 10% dry DMSO (100 µL) in anhydrous DCM (1 mL), 4-tert-butyl-benzene-sulfonyl chloride (10.1 mg) and diisopropylethylamine (20 µL) were added under Ar, and stirred 2 h at room temperature. Tris-(2-aminoethyl)-amine polystyrene (10 mg) and (polystyrylmethyl)trimethylammonium bicarbonate (10 mg) were added to the reaction mixture and agitated for 18 h at room temperature. The supernatant was separated from the resin by filtration, the polymeric beads were washed with DCM and a mixture of DCM/MeOH (1/1) (three times). After evaporation of

the solvent, the residue was purified by HPLC to give 3-naphthalen-2-yl-2-(4-tert-butyl-benzenesulfonylamino)-propionic acid cyanomethyl-amide (11.8 mg, 91%).

NMR-^{1}H (DMSO-d_6) δ = 1.19 (s, 9 H), 3.14 (m, 1 H), 3.62 (m, 3 H), 3.99 (m, 2 H), 7.13 (m, 1 H), 7.18-7.38 (m, 5 H), 7.46-7.52 (m, 3 H), 7.61 (m, 1 H), 7.71-7.88 (m, 3 H), 8.28 (m, 1 H), 8.78 (m, 1 H); MS: *m/z*: 450.2 [M^+].

EXAMPLE 7

1-Methyl-cyclopropanecarboxylic acid [1-(cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-amide



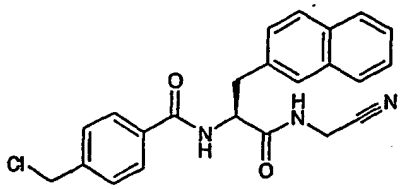
To a solution of PyBrOP (148.5 mg), 1-methylcyclopropane carboxylic acid (33.4 mg) and diisopropylethylamine (152 µL) in anhydrous DMF (1.1 mL) was added 1-hydroxybenzotriazole-6-sulfonamidomethyl polystyrene (113.8 mg). The mixture was reacted at room temperature for 5 h. After the first activation step the resin was washed with DMF (three times). The second activation step was performed under the same conditions as the first one, and the resin was washed with DMF (five times).

The amine salt (prepared as described in example 1) (30 mg) was added to a suspension of the resin in anhydrous DCM (1 mL) and diisopropylethylamine (152 µL). The polymer-bound activated ester was reacted with this mixture at room temperature. After 20 h, the supernatant was separated from the resin by filtration. The polymeric beads were washed with DCM and a mixture of DCM/MeOH (1/1) (three times). After evaporation of the solvent, the residue was purified by HPLC to give 1-methyl-cyclopropanecarboxylic acid [1-(cyanomethyl-carbamoyl)-2-naphthlen-2-yl-ethyl]-amide (38.9 mg, 98%).

NMR-^{1}H (DMSO-d_6) δ = 0.42 (m, 2 H), 0.79 (m, 2 H), 1.20 (s, 3 H), 3.10 (dd, 1 H, J = 9.8, J = 13.6 Hz), 3.20 (dd, 1 H, J = 4.9, J = 13.6 Hz, 1 H), 4.16 (m, 2 H), 4.57 (m, 1 H), 7.40-7.56 (m, 3 H), 7.73 (s, 1 H), 7.73-7.88 (m, 3 H), 8.66 (m, 1 H); MS: *m/z*: 336.0 [M^+].

EXAMPLE 8

4-Chloromethyl-*N*-[1-(cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-benzamide

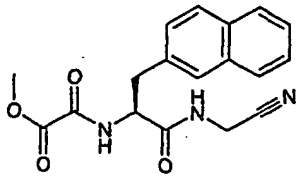


Amine salt (prepared as described in example 1) (30 mg) was dissolved in a mixture of 10% dry DMSO (100 µL) in anhydrous DCM (1 mL), 4-(chloromethyl)benzoyl chloride (27 mg) and diisopropylethylamine (103 µL) were added under Ar, and stirred for 2 h at room temperature. Tris-(2-aminoethyl)-amine polystyrene (40 mg) and (polystyrylmethyl)-trimethylammonium bicarbonate (40 mg) were added to the reaction mixture and agitated for 18 h at room temperature. The supernatant was separated from the resin by filtration, the polymeric beads were washed with DCM and a mixture of DCM/MeOH (1/1) (three times). After evaporation of the solvent, the residue was purified by HPLC to give 4-chloromethyl-*N*-[1-(cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-benzamide (30.3 mg, 86%).

NMR-^{1}H (DMSO-d_6) δ = 3.18 (m, 1 H), 3.30 (m, 1 H), 4.18 (m, 2 H), 4.78 (s, 2 H), 4.83 (m, 1 H), 7.40-7.62 (m, 5 H), 7.78-7.85 (m, 6 H), 8.82 (m, 1 H); MS: *m/z*: 405.9 [M^+].

EXAMPLE 9

***N*-[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-oxalamic acid methyl ester**

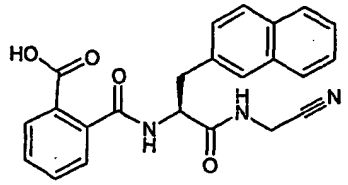


Amine salt (prepared as described in example 1) (30 mg) was dissolved in a mixture of 10% dry DMSO (100 µL) in anhydrous DCM (1 mL), mono-methyl oxalyl chloride (14 µL) and diisopropylethylamine (103 µL) were added under Ar, and stirred for 2 h at room temperature. Tris-(2-aminoethyl)-amine polystyrene (40 mg) and (polystyrylmethyl)trimethylammonium bicarbonate (40 mg) were added to the reaction mixture and agitated for 18 h at room temperature. The supernatant was separated from the resin by filtration, the polymeric beads were washed with DCM and a mixture of DCM/MeOH (1/1) (three times). After evaporation of the solvent, the residue was purified by HPLC to give *N*-[1-(cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-oxalamic acid methyl ester (25.1 mg, 85%).

NMR-^{1}H (DMSO-d_6) δ = 3.14 (dd, 1 H, J = 9.6, J = 14.0 Hz, 1 H), 3.29 (dd, 1 H, J = 4.9, J = 14.0 Hz, 1 H), 3.72 (s, 3 H), 4.17 (m, 2 H), 4.63 (m, 1 H), 7.13 (m, 1 H), 7.40-7.49 (m, 3 H), 7.73-7.87 (m, 4 H), 8.84 (m, 1 H), 9.14 (m, 1 H); MS: *m/z*: 340.0 [M^+].

EXAMPLE 10

N-[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-phthalamic acid

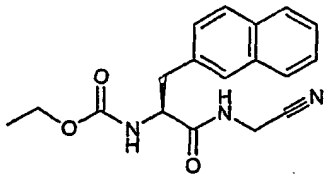


Amine salt (prepared as described in example 1) (30 mg) was dissolved in a mixture of 10% dry DMSO (100 µL) in anhydrous DCM (1 mL), phthalic anhydride (21 mg) and diisopropylethylamine (103 µL) were added under Ar, and stirred for 2 h at room temperature. Tris-(2-aminoethyl)-amine polystyrene (40 mg) and (polystyrylmethyl)-trimethylammonium bicarbonate (40 mg) were added to the reaction mixture and agitated for 18 h at room temperature. The supernatant was separated from the resin by filtration, the polymeric beads were washed with DCM and a mixture of DCM/MeOH (1/1) (three times). After evaporation of the solvent, the residue was purified by HPLC to give *N*-[1-(cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-phthalamic acid (28.6 mg, 82%).

NMR-^{1}H (DMSO-d_6) δ = 3.09 (dd, 1 H, J = 9.8, J = 14.0 Hz, 1 H), 3.35 (dd, 1 H, J = 5.1, J = 14.0 Hz, 1 H), 4.19 (m, 2 H), 4.75 (m, 1 H), 7.13 (m, 1 H), 7.45-7.51 (m, 5 H), 7.72-7.87 (m, 5 H), 8.55 (m, 1 H), 8.79 (d, J = 7.7 Hz, 1 H), 13.12 (bs, 1 H).; MS: *m/z*: 401.9 [M^+].

EXAMPLE 11

[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid ethyl ester

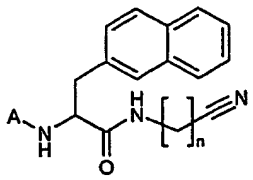


Amine salt (prepared as described in example 1) (30 mg) was dissolved in a mixture of 10% dry DMSO (100 µL) in anhydrous DCM (1 mL), ethyl chloroformate (14 µL) and

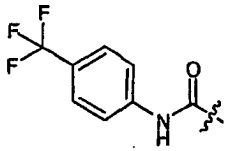
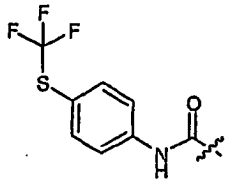
diisopropylethylamine (103 μL) were added under Ar, and stirred for 2 h at room temperature. Tris-(2-aminoethyl)-amine polystyrene (40 mg) was added to the reaction mixture and agitated for 18 h at room temperature. The supernatant was separated from the resin by filtration, the polymeric beads were washed with DCM and a mixture of DCM/MeOH (1/1) (three times). After evaporation of the solvent, the residue was purified by HPLC to give *N*-[1-(cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-phthalamic acid (25.5 mg, 90%).

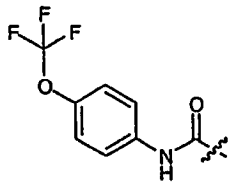
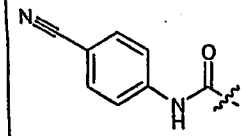
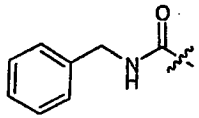
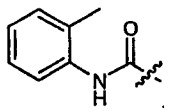
NMR-^{1}H (DMSO-d_6) δ = 1.04 (dd, 3 J = 7.5, J = 6.6 Hz H), 2.93 (dd, 1 H, J = 10.3, J = 13.7 Hz, 1 H), 3.14 (dd, 1 H, J = 4.5, J = 13.7 Hz, 1 H), 3.86 (m, 3 H), 4.15 (m, 2 H), 4.30 (m, 1 H), 7.43-7.51 (m, 3 H), 7.75-7.88 (m, 4 H), 8.76 (m, 1 H); MS: *m/z*: 326.0 [M^+].

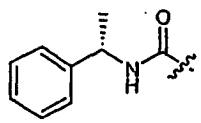
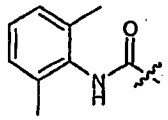
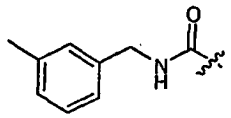
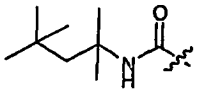
The following additional compounds of Formula I that can be prepared by the methods described in this application.

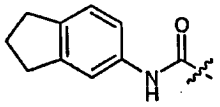
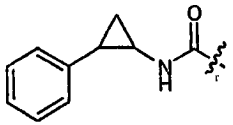
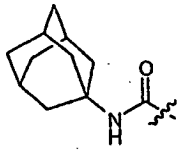
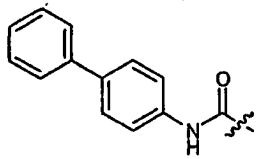
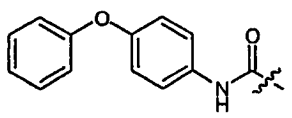


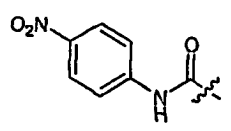
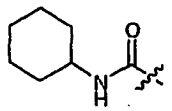
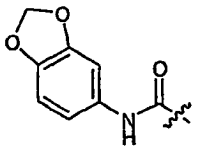
Column A lists the different A substituents:

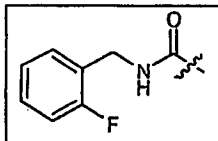
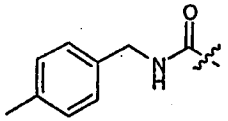
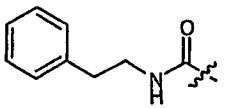
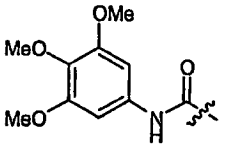
A	Name ^{1}H-NMR (DMSO-d_6, ppm)	Methods	MS Data
	**n = 1**; 3-Naphthalen-2-yl-2-acetylamino-propionic acid cyanomethyl-amide	A, B, H or I	*m/z*: 295.9 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-acetylamino-propionic acid cyanoethyl-amide	A, B, H or I	*m/z*: 309.9 [M^+]
	**n = 1**; 3-Naphthalen-2-yl-2-[3-(4-trifluoromethyl-phenyl)-ureido]-propionic acid cyanomethyl-amide	F or M	*m/z*: 440.9 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-[3-(4-trifluoromethyl-phenyl)-ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 454.9 [M^+]
	**n = 1**; 3-Naphthalen-2-yl-2-[3-(4-trifluoromethylsulfanyl-phenyl)-ureido]-propionic acid cyanomethyl-amide δ = 3.06 (dd, 1 H, J = 7.7, J = 13.7 Hz), 3.19 (dd, 1 H, J = 5.8, J = 13.7 Hz), 4.18 (m, 2 H), 4.60 (m, 1 H), 7.38 (m, 1 H), 7.43-7.52 (m, 4 H), 7.63 (m, 2 H), 7.70 (s, 1 H), 7.82-7.88 (m, 3 H), 8.90 (m, 1 H).	F or M	*m/z*: 472.9 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-[3-(4-trifluoromethylsulfanyl-phenyl)-ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 486.9 [M^+]

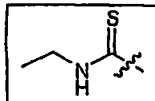
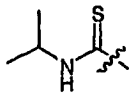
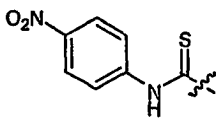
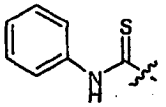
	**n = 1;** 3-Naphthalen-2-yl-2-[3-(4-trifluoromethoxy-phenyl)-ureido]-propionic acid cyanomethyl-amide δ = 3.08 (dd, 1 H, J = 7.8, J = 13.5 Hz), 3.16 (dd, 1 H, J = 5.5, J = 13.5 Hz), 4.17 (m, 2 H), 4.59 (m, 1 H), 6.48 (m, 1 H), 7.19 (m, 2 H), 7.28 (m, 2 H), 7.47-7.57 (m, 3 H), 7.70 (s, 1 H), 7.82-7.88 (m, 3 H), 8.87 (m, 1 H).	F or M	*m/z*: 457.0 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-[3-(4-trifluoromethoxy-phenyl)-ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 471.0 [M^+]
	**n = 1;** 3-Naphthalen-2-yl-2-[3-(4-cyano-phenyl)-ureido]-propionic acid cyanomethyl-amide	F or M	*m/z*: 398.0 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-[3-(4-cyano-phenyl)-ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 412.0 [M^+]
	**n = 1;** 3-Naphthalen-2-yl-2-(3-benzyl-ureido)-propionic acid cyanomethyl-amide	F or M	*m/z*: 387.0 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-(3-benzyl-ureido)-propionic acid cyanoethyl-amide	F or M	*m/z*: 401.0 [M^+]
	**n = 1;** 3-Naphthalen-2-yl-2-(3-o-tolyl-ureido)-propionic acid cyanomethyl-amide	F or M	*m/z*: 387.0 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-(3-o-tolyl-ureido)-propionic acid cyanoethyl-amide	F or M	*m/z*: 401.0 [M^+]

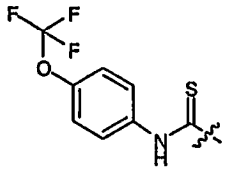
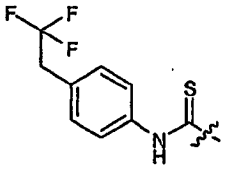
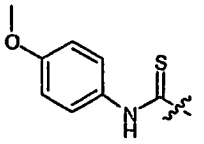
	**n = 1;** 3-Naphthalen-2-yl-2-[3-(*S*)-(1-phenyl-ethyl)-ureido]-propionic acid cyanomethyl-amide	F or M	*m/z*: 400.9 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-[3-(*S*)-(1-phenyl-ethyl)-ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 414.9 [M^+]
	**n = 1;** 3-Naphthalen-2-yl-2-[3-(2,6-dimethyl-phenyl)-ureido]-propionic acid cyanomethyl-amide. δ = 2,00, 2,01 (2 s , 6H), 3.00 (dd, 1 H, J = 8.2, J = 13.3Hz), 3.17 (dd, 1 H, J = 5.0, J = 13.3 Hz, 1 H), 4.18 (m, 2 H), 4.60 (m, 1 H), 6,97 (s, 3 H), 7.37 (m, 1 H), 7.49 (m, 2 H), 7.63 (s, 1 H), 7.79-7.88 (m, 3 H), 8.84 (m, 1 H).	F or M	*m/z*: 401.0 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-[3-(2,6-dimethyl-phenyl)-ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 414.9 [M^+]
	**n = 1;** 3-Naphthalen-2-yl-2-[3-(3-methyl-benzyl)-ureido]-propionic acid cyanomethyl-amide	F or M	*m/z*: 401.0 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-[3-(3-methyl-benzyl)-ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 414.9 [M^+]
	**n = 1;** 3-Naphthalen-2-yl-2-[3-(1,1,3,3-tetramethyl-butyl)-ureido]-propionic acid cyanomethyl-amide	F or M	*m/z*: 408.9 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-[3-(1,1,3,3-tetramethyl-butyl)-ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 422.9 [M^+]

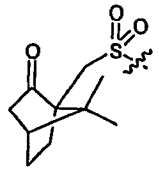
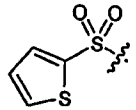
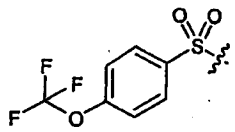
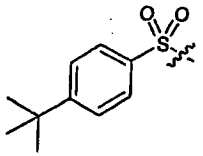
	**n = 1;** 3-Naphthalen-2-yl-2-(3-indan-5-yl-ureido)-propionic acid cyanomethyl-amide	F or M	*m/z*: 413.0 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-(3-indan-5-yl-ureido)-propionic acid cyanoethyl-amide	F or M	*m/z*: 427.0 [M^+]
	**n = 1;** 3-Naphthalen-2-yl-2-[3-(2-phenyl-cyclopropyl)-ureido]-propionic acid cyanomethyl-amide	F or M	*m/z*: 413.1 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-[3-(2-phenyl-cyclopropyl)-ureido]-propionic acid cyanoethyl-amide	E or K	*m/z*: 427.1 [M^+]
	**n = 1;** 3-Naphthalen-2-yl-2-(3-adamantan-1-yl-ureido)-propionic acid cyanomethyl-amide	F or M	*m/z*: 431.0 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-(3-adamantan-1-yl-ureido)-propionic acid cyanoethyl-amide	F or M	*m/z*: 445.0 [M^+]
	**n = 1;** 3-Naphthalen-2-yl-2-(3-biphenyl-4-yl-ureido)-propionic acid cyanomethyl-amide	F or M	*m/z*: 449.1 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-(3-biphenyl-4-yl-ureido)-propionic acid cyanoethyl-amide	F or M	*m/z*: 463.1 [M^+]
	**n = 1;** 3-Naphthalen-2-yl-2-[3-(4-phenoxy-phenyl)-ureido]-propionic acid cyanomethyl-amide	F or M	*m/z*: 465.0 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-[3-(4-phenoxy-phenyl)-ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 479.0 [M^+]

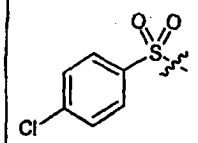
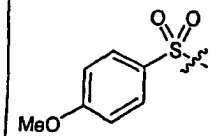
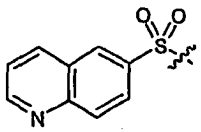
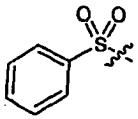
	**n = 1**; 3-Naphthalen-2-yl-2-[3-(4-nitro-phenyl)-ureido]-propionic acid cyanomethyl-amide	F or M	*m/z*: 418.0 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-[3-(4-nitro-phenyl)-ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 432.0 [M^+]
	**n = 1**; 3-Naphthalen-2-yl-2-(3-cyclohexyl-ureido)-propionic acid cyanomethyl-amide	F or M	*m/z*: 378.9 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-(3-cyclohexyl-ureido)-propionic acid cyanoethyl-amide	F or M	*m/z*: 392.9 [M^+]
	**n = 1**; 3-Naphthalen-2-yl-2-(3-benzo[1,3]dioxol-5-yl-ureido)-propionic acid cyanomethyl-amide δ = 3.03 (dd, 1 H, J = 7.5, J = 13.9 Hz, 1 H), 3.16 (dd, 1 H, J = 5.5, J = 13.9 Hz, 1 H), 4.16 (m, 2 H), 4.58 (m, 1 H), 5.91 (s, 2 H), 6.34 (d, 1 H, J = 8.4 Hz, 1 H), 6.60 (dd, 1 H, J = 2.0, J = 8.4 Hz, 1 H), 6.74 (d, 1 H, J = 8.4 Hz, 1 H), 7.09 (d, 1 H, J = 2.0 Hz, 1 H), 7.37 (m, 1 H), 7.36-7.48 (m, 2 H), 7.70 (s, 1 H), 7.81-7.88 (m, 3 H), 8.55 (s, 1 H), 8.84 (m, 1 H).	F or M	*m/z*: 417.0 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-(3-benzo[1,3]dioxol-5-yl-ureido)-propionic acid cyanoethyl-amide	F or M	*m/z*: 431.0 [M^+]
	n = 1; 3-Naphthalen-2-yl-2-[3-(2-fluoro-benzyl)-ureido]-propionic acid cyanomethyl-amide	F or M	*m/z*: 405.0 [M^+]

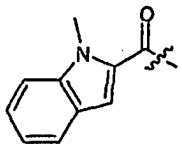
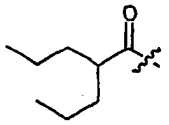
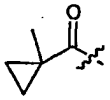
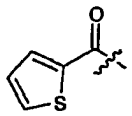
	**n = 2**; 3-Naphthalen-2-yl-2-[3-(2-fluoro-benzyl)-ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 419.0 [M^+]
	**n = 1**; 3-Naphthalen-2-yl-2-[3-(4-methyl-benzyl)-ureido]-propionic acid cyanomethyl-amide	F or M	*m/z*: 401.0 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-[3-(4-methyl-benzyl)-ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 415.0 [M^+]
	**n = 1**; 3-Naphthalen-2-yl-2-(3-phenethyl-ureido) -ureido]-propionic acid cyanomethyl-amide δ = 2.58 (dd, 2 H, J = 7.2, J = 7.4 Hz), 2.93 (dd, 1 H, J = 8.5, J = 13.7 Hz), 3.07 (m, 1 H), 3.14 (m, 2 H), 4.13 (m, 1 H), 4.49 (m, 1 H), 6.07 (m, 1 H), 6.22 (m, 1 H), 7.11-7.26 (m, 5 H), 7.35 (m, 1 H), 7.47 (m, 2 H), 7.67 (s, 1 H), 7.80-7.88 (m, 3 H), 8.73 (m, 1 H).	F or M	*m/z*: 401.0 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-(3-phenethyl-ureido) -ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 415.0 [M^+]
	**n = 1**; 3-Naphthalen-2-yl-2-[3-(3,4,5-trimethoxy-phenyl)-ureido]-propionic acid cyanomethyl-amide	F or M	*m/z*: 463.0 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-[3-(3,4,5-trimethoxy-phenyl)-ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 477.0 [M^+]
	n = 1; 3-Naphthalen-2-yl-2-(3-ethyl-thioureido)-propionic acid cyanomethyl-amide	G or N	*m/z*: 340.9 [M^+]

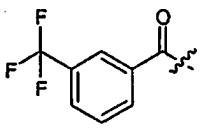
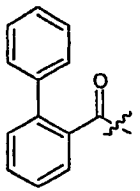
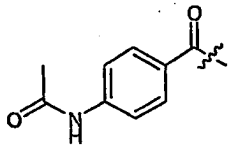
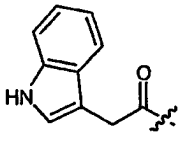
	**n = 2**; 3-Naphthalen-2-yl-2-(3-ethyl-thioureido)-propionic acid cyanoethyl-amide	G or N	*m/z*: 354.9 [M^+]
	**n = 1**; 3-Naphthalen-2-yl-2-(3-isopropyl-thioureido)-propionic acid cyanomethyl-amide	G or N	*m/z*: 355.0 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-(3-isopropyl-thioureido)-propionic acid cyanoethyl-amide	G or N	*m/z*: 369.0 [M^+]
	**n = 1**; 3-Naphthalen-2-yl-2-[3-(4-nitro-phenyl)-thioureido]-propionic acid cyanomethyl-amide	G or N	*m/z*: 433.9 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-[3-(4-nitro-phenyl)-thioureido]-propionic acid cyanoethyl-amide	G or N	*m/z*: 447.9 [M^+]
	**n = 1**; 3-Naphthalen-2-yl-2-(3-phenyl-thioureido)-propionic acid cyanomethyl-amide δ = 3.21 (m, 1 H), 3.29 (m, 1 H), 4.18 (m, 2 H), 5.26 (m, 1 H), 7.09 (m, 1 H), 7.26 (m, 2 H), 7.36 (m, 3 H), 7.49 (m, 2 H), 7.69 (s, 1 H), 7.82-7.90 (m, 3 H), 8.92 (m, 1 H), 9.82 (s, 1 H).	G or N	*m/z*: 388.9 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-(3-phenyl-thioureido)-propionic acid cyanoethyl-amide	G or N	*m/z*: 402.9 [M^+]

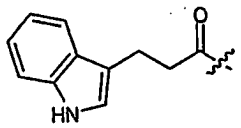
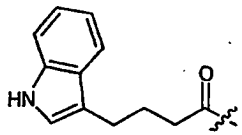
	**n = 1;** 3-Naphthalen-2-yl-2-[3-(4-trifluoromethoxy-phenyl)-thioureido]-propionic acid cyanomethyl-amide δ = 3.20 (m, 1 H), 3.29 (m, 1 H), 4.18 (m, 2 H), 5.25 (m, 1 H), 7.24 (m, 2 H), 7.38 (m, 1 H), 7.44-7.54 (m, 4 H), 7.70 (s, 1 H), 7.82-7.90 (m, 3 H), 8.93 (m, 1 H), 9.92 (s, 1 H).	G or N	*m/z*: 472.9 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-[3-(4-trifluoromethoxy-phenyl)-thioureido]-propionic acid cyanoethyl-amide	G or N	*m/z*: 486.9 [M^+]
	**n = 1;** 3-Naphthalen-2-yl-2-{3-[4-(2,2,2-trifluoro-ethyl)-phenyl]-thioureido}-propionic acid cyanomethyl-amide	G or N	*m/z*: 456.9 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-{3-[4-(2,2,2-trifluoro-ethyl)-phenyl]-thioureido}-propionic acid cyanoethyl-amide	G or N	*m/z*: 470.9 [M^+]
	**n = 1;** 3-Naphthalen-2-yl-2-[3-(4-methoxy-phenyl)-thioureido]-propionic acid cyanomethyl-amide δ = 3.21 (m, 1 H), 3.29 (m, 1 H), 3.72 (s, 3 H), 4.17 (m, 2 H), 5.25 (m, 1 H), 6.81 (m, 1 H), 7.16 (m, 2 H), 7.34 (m, 1 H), 7.49 (m, 2 H), 7.66 (s, 1 H), 7.82-7.90 (m, 3 H), 8.86 (m, 1 H), 9.64 (s, 1 H).	G or N	*m/z*: 419.0 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-[3-(4-methoxy-phenyl)-thioureido]-propionic acid cyanoethyl-amide	G or N	*m/z*: 433.0 [M^+]

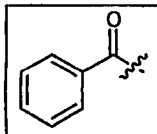
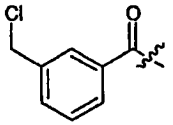
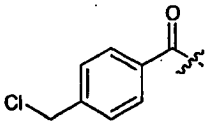
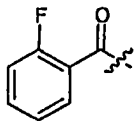
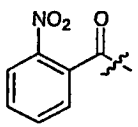
	**n = 1;** 3-Naphthalen-2-yl-2-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-ylmethanesulfonylamino)-propionic acid cyanomethyl-amide	E or L	*m/z*: 468.2 $[M^+]$
	n = 2; 3-Naphthalen-2-yl-2-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-ylmethanesulfonylamino)-propionic acid cyanoethyl-amide	E or L	*m/z*: 482.2 $[M^+]$
	**n = 1;** 3-Naphthalen-2-yl-2-(thiophene-2-sulfonylamino)-propionic acid cyanomethyl-amide	E or L	*m/z*: 400.0 $[M^+]$
	n = 2; 3-Naphthalen-2-yl-2-(thiophene-2-sulfonylamino)-propionic acid cyanoethyl-amide	E or L	*m/z*: 414.0 $[M^+]$
	**n = 1;** 3-Naphthalen-2-yl-2-(4-trifluoromethoxy-benzenesulfonylamino)-propionic acid cyanomethyl-amide	E or L	*m/z*: 478.1 $[M^+]$
	n = 2; 3-Naphthalen-2-yl-2-(4-trifluoromethoxy-benzenesulfonylamino)-propionic acid cyanoethyl-amide	E or L	*m/z*: 492.1 $[M^+]$
	**n = 1;** 3-Naphthalen-2-yl-2-(4-*tert*-butyl-benzenesulfonylamino)-propionic acid cyanomethyl-amide δ = 1.19 (s, 9 H), 3.14 (m, 1 H), 3.62 (m, 3 H), 3.99 (m, 2 H), 7.13 (m, 1 H), 7.18-7.38 (m, 5 H), 7.46-7.52 (m, 3 H), 7.61 (m, 1 H), 7.71-7.88 (m, 3 H), 8.28 (m, 1 H), 8.78 (m, 1 H).	E or L	*m/z*: 450.2 $[M^+]$
	n = 2; 3-Naphthalen-2-yl-2-(4-*tert*-butyl-benzenesulfonylamino)-propionic acid cyanoethyl-amide	E or L	*m/z*: 464.2 $[M^+]$

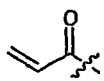
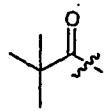
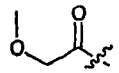
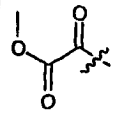
	**n = 1**; 3-Naphthalen-2-yl-2-(4-chloro-benzenesulfonylamino)-propionic acid cyanomethyl-amide	E or L	*m/z*: 428.1 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-(4-chloro-benzenesulfonylamino)-propionic acid cyanoethyl-amide	E or L	*m/z*: 442.1 [M^+]
	**n = 1**; 3-Naphthalen-2-yl-2-(4-methoxy-benzenesulfonylamino)-propionic acid cyanomethyl-amide	E or L	*m/z*: 424.1 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-(4-methoxy-benzenesulfonylamino)-propionic acid cyanoethyl-amide	E or L	*m/z*: 438.1 [M^+]
	**n = 1**; 3-Naphthalen-2-yl-2-(quinoline-6-sulfonylamino)-propionic acid cyanomethyl-amide	E or L	*m/z*: 445.2 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-(quinoline-6-sulfonylamino)-propionic acid cyanoethyl-amide	E or L	*m/z*: 459.2 [M^+]
	**n = 1**; 3-Naphthalen-2-yl-2-benzenesulfonylamino-propionic acid cyanomethyl-amide δ = 2.80 (dd, 1 H, J = 9.2, J = 13.5Hz), 3.02 (dd, 1 H, J = 5.7, J = 13.5 Hz, 1 H), 3.97 (m, 2 H), 4.03 (m, 1 H), 7.23 (m, 3 H), 7.37 (m, 1 H), 7.45-7.51 (m, 4 H), 7.58 (s, 1 H), 7.70-7.85 (m, 3 H), 8.34 (m, 1 H).	E or L	*m/z*: 394.1 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-benzenesulfonylamino-propionic acid cyanoethyl-amide	E or L	*m/z*: 408.1 [M^+]

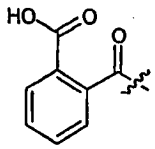
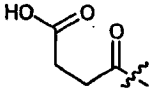
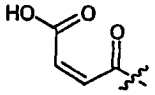
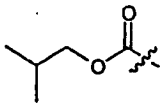
	**n = 1**; 1-Methyl-1H-indole-2-carboxylic acid [1-(cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-amide	D or K	*m/z*: 411.1 [M^+]
	n = 2; 1-Methyl-1H-indole-2-carboxylic acid [1-(cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-amide	D or K	*m/z*: 425.0 [M^+]
	**n = 1**; 2-Propyl-pentanoic acid [1-(cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-amide	D or K	*m/z*: 380.1 [M^+]
	n = 2; 2-Propyl-pentanoic acid [1-(cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-amide	D or K	*m/z*: 394.0 [M^+]
	**n = 1**; 1-Methyl-cyclopropanecarboxylic acid [1-(cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-amide δ = 0.42 (m, 2 H), 0.79 (m, 2 H), 1.20 (s, 3 H), 3.10 (dd, 1 H, J = 9.8, J = 13.6 Hz), 3.20 (dd, 1 H, J = 4.9, J = 13.6 Hz, 1 H), 4.16 (m, 2 H), 4.57 (m, 1 H), 7.40-7.56 (m, 3 H), 7.73 (s, 1 H), 7.73-7.88 (m, 3 H), 8.66 (m, 1 H).	D or K	*m/z*: 336.0 [M^+]
	n = 2; 1-Methyl-cyclopropanecarboxylic acid [1-(cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-amide	D or K	*m/z*: 350.0 [M^+]
	**n = 1**; Thiophene-2-carboxylic acid [1-(cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-amide	D or K	*m/z*: 363.9 [M^+]
	n = 2; Thiophene-2-carboxylic acid [1-(cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-amide	D or K	*m/z*: 377.9 [M^+]

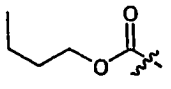
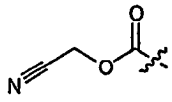
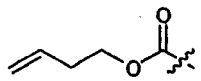
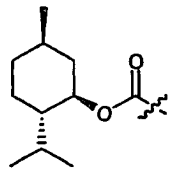
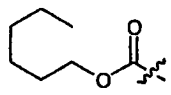
	**n = 1**; *N*-[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-3-trifluoromethyl-benzamide	D or K	*m/z*: 425.9 [M^+]
	n = 2; *N*-[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-3-trifluoromethyl-benzamide	D or K	*m/z*: 439.9 [M^+]
	**n = 1**; Biphenyl-2-carboxylic acid [1-(cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-amide	D or K	*m/z*: 434.0 [M^+]
	n = 2; Biphenyl-2-carboxylic acid [1-(cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-amide	D or K	*m/z*: 448.0 [M^+]
	**n = 1**; 4-Acetylamino-*N*-[1-(cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-benzamide	D or K	*m/z*: 415.0 [M^+]
	n = 2; 4-Acetylamino-*N*-[1-(cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-benzamide	D or K	*m/z*: 429.0 [M^+]
	**n = 1**; 3-Naphthalen-2-yl-2-(2-1*H*-indol-3-yl-acetylamino)-propionic acid cyanomethyl-amide δ = 2.99 (dd, 1 H, J = 8.9, J = 13.5 Hz), 3.15 (dd, 1 H, J = 5.1, J = 13.5 Hz), 3.51 (s, 2 H), 4.14 (m, 2 H), 4.59 (m, 1 H), 6.69 (m, 1 H), 6.98 (m, 1 H), 7.07 (s, 1 H), 7.25 (m, 2 H), 7.35 (m, 1 H), 7.43-7.48 (m, 2 H), 7.68 (s, 1 H), 7.75 (m, 2 H), 7.85 (m, 1 H), 8.29 (m, 1 H), 8.79 (m, 1 H).	D or K	*m/z*: 411.1 [M^+]

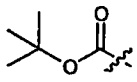
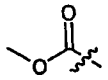
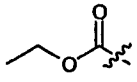
	n = 2; 3-Naphthalen-2-yl-2-(2-1*H*-indol-3-yl-acetylamino)-propionic acid cyanoethyl-amide	D or K	*m/z*: 426.0 [M^+]
	**n = 1;** 3-Naphthalen-2-yl-2-(3-1*H*-indol-3-yl-propionylamino)-propionic acid cyanomethyl-amide δ = 2.42 (m, 2 H), 2.74 (m, 2 H), 2.94 (dd, 1 H, J = 9.3, J = 13.7 Hz), 3.15 (m, 1 H), 4.14 (m, 2 H), 4.64 (m, 1 H), 6.94 (m, 1 H), 7.01 (m, 2 H), 7.10 (m, 1 H), 7.31 (m, 1 H), 7.38-7.49 (m, 3 H), 7.71 (s, 1 H), 7.79 (m, 2 H), 7.86 (m, 1 H), 8.30 (m, 1 H), 8.75 (m, 1 H).	D or K	*m/z*: 425.0 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-(3-1*H*-indol-3-yl-propionylamino)-propionic acid cyanoethyl-amide	D or K	*m/z*: 439.0 [M^+]
	**n = 1;** *N*-[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-4-(1*H*-indol-3-yl)-butyramide δ = 1.70 (m, 2 H), 2.11 (m, 2 H), 2.47 (m, 2 H), 2.94 (dd, 1 H, J = 9.3, J = 13.7 Hz), 3.15 (m, 1 H), 4.14 (m, 2 H), 4.64 (m, 1 H), 6.92 (m, 2 H), 7.03 (m, 2 H), 7.31 (m, 1 H), 7.37-7.49 (m, 3 H), 7.72 (s, 1 H), 7.75-7.85 (m, 4 H), 8.22 (m, 1 H), 8.75 (m, 1 H).	D or K	*m/z*: 439.0 [M^+]
	n = 2; *N*-[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-4-(1*H*-indol-3-yl)-butyramide	D or K	*m/z*: 453.0 [M^+]
	n = 1; N-[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-benzamide	D or K	*m/z*: 358.0 [M^+]

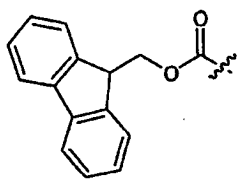
	**n = 2;** N-[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-benzamide	D or K	*m/z*: 372.0 [M^+]
	**n = 1;** 3-Chloromethyl-*N*-[1-(cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-benzamide	D or K	*m/z*: 406.0 [M^+]
	n = 2; 3-Chloromethyl-*N*-[1-(cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-benzamide	D or K	*m/z*: 420.0 [M^+]
	**n = 1;** 4-Chloromethyl-*N*-[1-(cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-benzamide δ = 3.13 (m, 1 H), 3.30 (m, 1 H), 4.18 (m, 2 H), 4.78 (s, 2 H), 4.83 (m, 1 H), 7.40-7.62 (m, 5 H), 7.78-7.85 (m, 6 H), 8.82 (m, 1 H).	D or K	*m/z*: 405.9 [M^+]
	n = 2; 4-Chloromethyl-*N*-[1-(cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-benzamide	D or K	*m/z*: 420.0 [M^+]
	**n = 1;** *N*-[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-2-fluoro-benzamide	D or K	*m/z*: 375.9 [M^+]
	n = 2; *N*-[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-2-fluoro-benzamide	D or K	*m/z*: 389.9 [M^+]
	**n = 1;** *N*-[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-2-nitro-benzamide	D or K	*m/z*: 402.9 [M^+]
	n = 2; *N*-[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-2-nitro-benzamide	D or K	*m/z*: 416.9 [M^+]

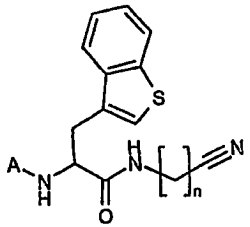
	**n = 1**; *N*-[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-acrylamide	D or K	*m/z*: 307.9 [M^+]
	n = 2; *N*-[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-acrylamide	D or K	*m/z*: 321.9 [M^+]
	**n = 1**; 3-Naphthalen-2-yl-2,2-dimethyl-propionic acid cyanomethyl-amide	D or K	*m/z*: 338.0 [M^+]
	n = 2; 3-Naphthalen-2-yl-2,2-dimethyl-propionic acid cyanoethyl-amide	D or K	*m/z*: 352.0 [M^+]
	**n = 1**; 3-Naphthalen-2-yl-2-(2-methoxy-acetylamino)-propionic acid cyanomethyl-amide	D or K	*m/z*: 326.0 [M^+]
	n = 2; 3-Naphthalen-2-yl-2-(2-methoxy-acetylamino)-propionic acid cyanoethyl-amide	D or K	*m/z*: 340.0 [M^+]
	**n = 1**; *N*-[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-oxalamic acid methyl ester δ = 3.14 (dd, 1 H, J = 9.6, J = 14.0 Hz), 3.29 (dd, 1 H, J = 4.9, J = 14.0 Hz), 3.72 (s, 3 H), 4.17 (m, 2 H), 4.63 (m, 1 H), 7.13 (m, 1 H), 7.40-7.49 (m, 3 H), 7.73-7.87 (m, 4 H), 8.84 (m, 1 H), 9.14 (m, 1 H).		*m/z*: 340.0 [M^+]
	n = 2; *N*-[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-oxalamic acid methyl ester		*m/z*: 354.0 [M^+]

	**n** = 1; *N*-[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-phthalamic acid δ = 3.09 (dd, 1 H, J = 9.8, J = 14.0 Hz), 3.35 (dd, 1 H, J = 5.1, J = 14.0 Hz), 4.19 (m, 2 H), 4.75 (m, 1 H), 7.13 (m, 1 H), 7.45-7.51 (m, 5 H), 7.72-7.87 (m, 5 H), 8.55 (m, 1 H), 8.79 (d, J = 7.7 Hz, 1 H), 13.12 (bs, 1 H).	B or I	*m/z*: 401.9 [M^+]
	n = 2; *N*-[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-phthalamic acid	B or I	*m/z*: 415.9 [M^+]
	**n** = 1; *N*-[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-succinamic acid	B or I	*m/z*: 353.9 [M^+]
	n = 2; *N*-[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-succinamic acid	B or I	*m/z*: 367.9 [M^+]
	**n** = 1; 3-[1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethylcarbamoyl]-acrylic acid	B or I	*m/z*: 352.0 [M^+]
	n = 2; 3-[1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethylcarbamoyl]-acrylic acid	B or I	*m/z*: 366.0 [M^+]
	**n** = 1; [1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid isobutyl ester	C or J	*m/z*: 354.0 [M^+]
	n = 2; [1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid isobutyl ester	C or J	*m/z*: 368.0 [M^+]

	**n = 1;** [1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid butyl ester	C or J	*m/z*: 354.0 [M^+]
	n = 1; [1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid butyl ester	C or J	*m/z*: 368.0 [M^+]
	**n = 1;** [1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid cyanomethyl ester	C or J	*m/z*: 335.9 [M^+]
	n = 2; [1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid cyanomethyl ester	C or J	*m/z*: 349.9 [M^+]
	**n = 1;** [1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid but-3-enyl ester	C or J	*m/z*: 352.0 [M^+]
	n = 2; [1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid but-3-enyl ester	C or J	*m/z*: 366.0 [M^+]
	**n = 1;** [1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid 2-isopropyl-5-methyl-cyclohexyl ester	C or J	*m/z*: 436.0 [M^+]
	n = 2; [1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid 2-isopropyl-5-methyl-cyclohexyl ester	C or J	*m/z*: 450.0 [M^+]
	**n = 1;** [1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid hexyl ester	C or J	*m/z*: 382.0 [M^+]
	n = 2; [1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid hexyl ester	C or J	*m/z*: 396.0 [M^+]

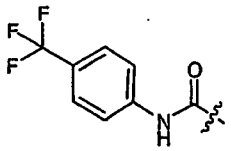
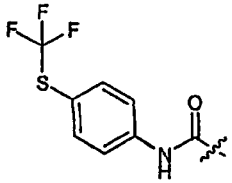
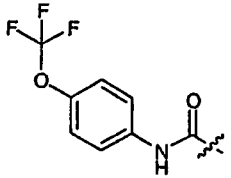
	**n = 1**; [1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid *tert*-butyl ester δ = 1.24 (s, 9 H), 2.93 (dd, 1 H, J = 10.2, J = 13.7 Hz), 3.14 (dd, 1 H, J = 4.6, J = 13.7 Hz), 4.14 (m, 2 H), 4.27 (m, 1 H), 7.13 (d, 1 H, J = 8.3 Hz), 7.42-7.50 (m, 3 H), 7.72-7.87 (m, 3 H), 8.68 (m, 1 H).		*m/z*: 353.9 [M^+]
	n = 2; [1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid *tert*-butyl ester δ = 1.24 (s, 9 H), 2.61 (m, 2 H), 2.93 (dd, 1 H, J = 10.3, J = 13.7 Hz), 3.13 (dd, 1 H, J = 4.3, J = 13.7 Hz), 3.37 (m, 2 H), 4.24 (m, 1 H), 6.99 (d, 1 H, J = 8.6 Hz), 7.43-7.50 (m, 3 H), 7.73-7.87 (m, 3 H), 8.33 (m, 1 H).		*m/z*: 367.8 [M^+]
	**n = 1**; [1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid methyl ester	C or J	*m/z*: 312.0 [M^+]
	n = 2; [1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid methyl ester	C or J	*m/z*: 326.0 [M^+]
	**n = 1**; [1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid ethyl ester δ = 1.04 (dd, 3 H, J = 7.5, J = 6.6 Hz), 2.93 (dd, 1 H, J = 10.3, J = 13.7 Hz), 3.14 (dd, 1 H, J = 4.5, J = 13.7 Hz), 3.86 (m, 3 H), 4.15 (m, 2 H), 4.30 (m, 1 H), 7.43-7.51 (m, 3 H), 7.75-7.88 (m, 4 H), 8.76 (m, 1 H).	C or J	*m/z*: 326.0 [M^+]

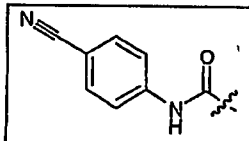
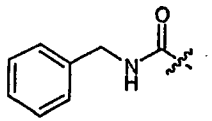
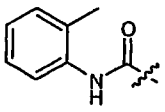
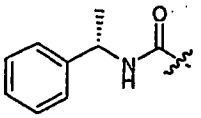
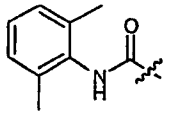
	n = 2; [1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid ethyl ester	C or J	*m/z*: 340.0 [M^+]
	**n** = 1; [1-(Cyanomethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid 9*H*-fluoren-9-ylmethyl ester	C or J	*m/z*: 475.9 [M^+]
	n = 2; [1-(Cyanoethyl-carbamoyl)-2-naphthalen-2-yl-ethyl]-carbamic acid 9*H*-fluoren-9-ylmethylester	C or J	*m/z*: 489.9 [M^+]

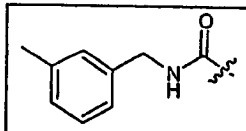
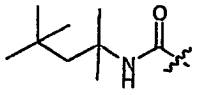
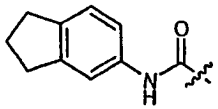
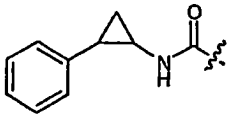
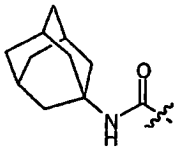


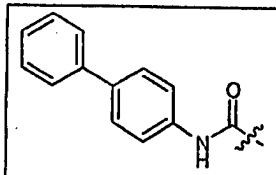
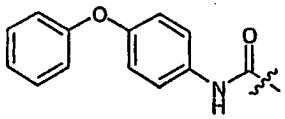
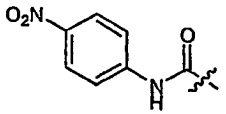
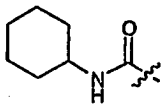
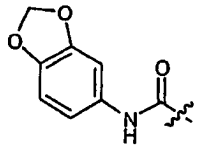
Column A lists the different A substituents:

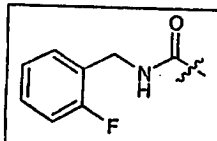
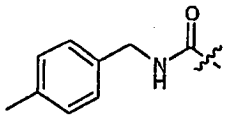
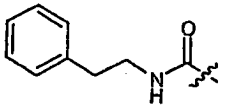
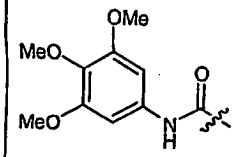
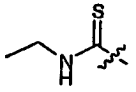
A	Name **^{1}H-NMR (DMSO-d_6, ppm)**	**Methods**	**MS Data**
	n = 1; 3-Benzo[b]thiophen-3-yl-2-acetylamino-propionic acid cyanomethyl-amide	A, B, H or I	*m/z*: 301.9 [M^+]

	**n = 2**; 3-Benzo[b]thiophen-3-yl-2-acetylamino-propionic acid cyanoethyl-amide δ = 1.78 (s, 3 H), 2.60 (m, 2 H), 3.03 (dd, 1 H, J = 9.3, J = 14.7 Hz), 3.22 (m, 1 H), 3.28 (m, 2 H), 4.58 (m, 1 H), 7.34-7.44 (m, 3 H), 7.89-7.98 (m, 2 H), 8.22 (m, 1 H), 8.44 (m, 1 H).	A, B, H or I	*m/z*: 315.9 [M^+]
	**n = 1**; 3-Benzo[b]thiophen-3-yl-2-[3-(4-trifluoromethyl-phenyl)-ureido]-propionic acid cyanomethyl-amide	F or M	*m/z*: 446.9 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-[3-(4-trifluoromethyl-phenyl)-ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 460.9 [M^+]
	**n = 1**; 3-Benzo[b]thiophen-3-yl-2-[3-(4-trifluoromethylsulfanyl-phenyl)-ureido]-propionic acid cyanomethyl-amide	F or M	*m/z*: 478.9 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-[3-(4-trifluoromethylsulfanyl-phenyl)-ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 492.9 [M^+]
	**n = 1**; 3-Benzo[b]thiophen-3-yl-2-[3-(4-trifluoromethoxy-phenyl)-ureido]-propionic acid cyanomethyl-amide	F or M	*m/z*: 463.0 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-[3-(4-trifluoromethoxy-phenyl)-ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 477.0 [M^+]
	n = 1; 3-Benzo[b]thiophen-3-yl-2-[3-(4-cyano-phenyl)-ureido]-propionic acid cyanomethyl-amide	F or M	*m/z*: 404.0 [M^+]

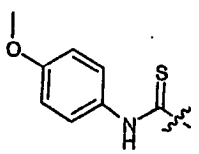
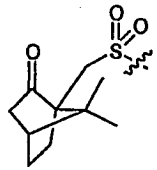
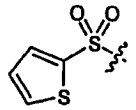
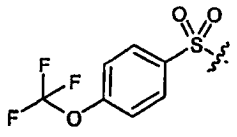
	**n = 2;** 3-Benzo[b]thiophen-3-yl-2-[3-(4-cyano-phenyl)-ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 418.0 [M^+]
	**n = 1;** 3-Benzo[b]thiophen-3-yl-2-(3-benzyl-ureido)-propionic acid cyanomethyl-amide	F or M	*m/z*: 393.0 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-(3-benzyl-ureido)-propionic acid cyanoethyl-amide	F or M	*m/z*: 407.0 [M^+]
	**n = 1;** 3-Benzo[b]thiophen-3-yl-2-(3-*o*-tolyl-ureido)-propionic acid cyanomethyl-amide	F or M	*m/z*: 393.0 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-(3-*o*-tolyl-ureido)-propionic acid cyanoethyl-amide	F or M	*m/z*: 407.0 [M^+]
	**n = 1;** 3-Benzo[b]thiophen-3-yl-2-[3-(*S*)-(1-phenyl-ethyl)-ureido]-propionic acid cyanomethyl-amide	F or M	*m/z*: 406.9 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-[3-(*S*)-(1-phenyl-ethyl)-ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 420.9 [M^+]
	**n = 1;** 3-Benzo[b]thiophen-3-yl-2-[3-(2,6-dimethyl-phenyl)-ureido]-propionic acid cyanomethyl-amide.	F or M	*m/z*: 407.0 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-[3-(2,6-dimethyl-phenyl)-ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 420.9 [M^+]
	n = 1; 3-Benzo[b]thiophen-3-yl-2-[3-(3-methyl-benzyl)-ureido]-propionic acid cyanomethyl-amide	F or M	*m/z*: 407.0 [M^+]

	n = 2; 3-Benzo[b]thiophen-3-yl-2-[3-(3-methyl-benzyl)-ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 420.9 [M^+]
	n = 1; 3-Benzo[b]thiophen-3-yl-2-[3-(1,1,3,3-tetramethyl-butyl)-ureido]-propionic acid cyanomethyl-amide	F or M	*m/z*: 414.9 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-[3-(1,1,3,3-tetramethyl-butyl)-ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 428.9 [M^+]
	n = 1; 3-Benzo[b]thiophen-3-yl-2-(3-indan-5-yl-ureido)-propionic acid cyanomethyl-amide	F or M	*m/z*: 419.0 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-(3-indan-5-yl-ureido)-propionic acid cyanoethyl-amide	F or M	*m/z*: 433.0 [M^+]
	n = 1; 3-Benzo[b]thiophen-3-yl-2-[3-(2-phenyl-cyclopropyl)-ureido]-propionic acid cyanomethyl-amide	F or M	*m/z*: 419.1 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-[3-(2-phenyl-cyclopropyl)-ureido]-propionic acid cyanoethyl-amide	E or K	*m/z*: 433.1 [M^+]
	n = 1; 3-Benzo[b]thiophen-3-yl-2-(3-adamantan-1-yl-ureido)-propionic acid cyanomethyl-amide	F or M	*m/z*: 437.0 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-(3-adamantan-1-yl-ureido)-propionic acid cyanoethyl-amide	F or M	*m/z*: 451.0 [M^+]
	n = 1; 3-Benzo[b]thiophen-3-yl-2-(3-biphenyl-4-yl-ureido)-propionic acid cyanomethyl-amide	F or M	*m/z*: 455.1 [M^+]

	**n = 2;** 3-Benzo[b]thiophen-3-yl-2-(3-biphenyl-4-yl-ureido)-propionic acid cyanoethyl-amide	F or M	*m/z*: 469.1 [M^+]
	**n = 1;** 3-Benzo[b]thiophen-3-yl-2-[3-(4-phenoxy-phenyl)-ureido]-propionic acid cyanomethyl-amide	F or M	*m/z*: 471.0 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-[3-(4-phenoxy-phenyl)-ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 485.0 [M^+]
	**n = 1;** 3-Benzo[b]thiophen-3-yl-2-[3-(4-nitro-phenyl)-ureido]-propionic acid cyanomethyl-amide	F or M	*m/z*: 424.0 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-[3-(4-nitro-phenyl)-ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 438.0 [M^+]
	**n = 1;** 3-Benzo[b]thiophen-3-yl-2-(3-cyclohexyl-ureido)-propionic acid cyanomethyl-amide	F or M	*m/z*: 384.9 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-(3-cyclohexyl-ureido)-propionic acid cyanoethyl-amide	F or M	*m/z*: 398.9 [M^+]
	**n = 1;** 3-Benzo[b]thiophen-3-yl-2-(3-benzo[1,3]dioxol-5-yl-ureido)-propionic acid cyanomethyl-amide	F or M	*m/z*: 423.0 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-(3-benzo[1,3]dioxol-5-yl-ureido)-propionic acid cyanoethyl-amide	F or M	*m/z*: 437.0 [M^+]
	n = 1; 3-Benzo[b]thiophen-3-yl-2-[3-(2-fluoro-benzyl)-ureido]-propionic acid cyanomethyl-amide	F or M	*m/z*: 411.0 [M^+]

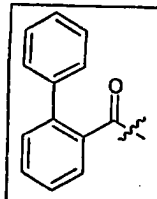
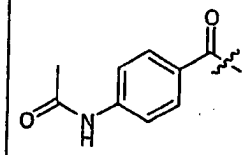
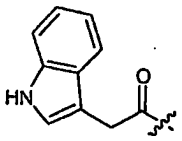
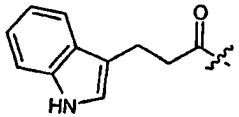
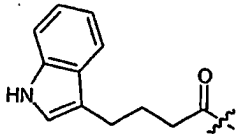
	**n = 2;** 3-Benzo[b]thiophen-3-yl-2-[3-(2-fluoro-benzyl)-ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 425.0 [M^+]
	**n = 1;** 3-Benzo[b]thiophen-3-yl-2-[3-(4-methyl-benzyl)-ureido]-propionic acid cyanomethyl-amide	F or M	*m/z*: 407.0 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-[3-(4-methyl-benzyl)-ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 421.0 [M^+]
	**n = 1;** 3-Benzo[b]thiophen-3-yl-2-(3-phenethyl-ureido) -ureido]-propionic acid cyanomethyl-amide	F or M	*m/z*: 407.0 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-(3-phenethyl-ureido) -ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 421.0 [M^+]
	**n = 1;** 3-Benzo[b]thiophen-3-yl-2-[3-(3,4,5-trimethoxy-phenyl)-ureido]-propionic acid cyanomethyl-amide	F or M	*m/z*: 469.0 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-[3-(3,4,5-trimethoxy-phenyl)-ureido]-propionic acid cyanoethyl-amide	F or M	*m/z*: 483.0 [M^+]
	**n = 1;** 3-Benzo[b]thiophen-3-yl-2-(3-ethyl-thioureido)-propionic acid cyanomethyl-amide	G or N	*m/z*: 346.9 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-(3-ethyl-thioureido)-propionic acid cyanoethyl-amide	G or N	*m/z*: 360.9 [M^+]
	n = 1; 3-Benzo[b]thiophen-3-yl-2-(3-isopropyl-thioureido)-propionic acid cyanomethyl-amide	G or N	*m/z*: 361.0 [M^+]

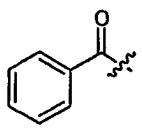
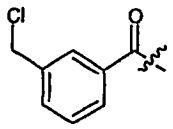
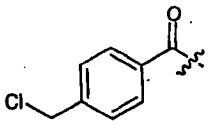
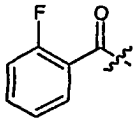
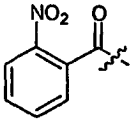
	n = 2; 3-Benzo[b]thiophen-3-yl-2-(3-isopropyl-thioureido)-propionic acid cyanoethyl-amide	G or N	*m/z*: 375.0 [M^+]
	n = 1; 3-Benzo[b]thiophen-3-yl-2-[3-(4-nitro-phenyl)-thioureido]-propionic acid cyanomethyl-amide	G or N	*m/z*: 439.9 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-[3-(4-nitro-phenyl)-thioureido]-propionic acid cyanoethyl-amide	G or N	*m/z*: 453.9 [M^+]
	n = 1; 3-Benzo[b]thiophen-3-yl-2-(3-phenyl-thioureido)-propionic acid cyanomethyl-amide	G or N	*m/z*: 394.9 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-(3-phenyl-thioureido)-propionic acid cyanoethyl-amide	G or N	*m/z*: 408.9 [M^+]
	n = 1; 3-Benzo[b]thiophen-3-yl-2-[3-(4-trifluoromethoxy-phenyl)-thioureido]-propionic acid cyanomethyl-amide	G or N	*m/z*: 478.9 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-[3-(4-trifluoromethoxy-phenyl)-thioureido]-propionic acid cyanoethyl-amide	G or N	*m/z*: 492.9 [M^+]
	n = 1; 3-Benzo[b]thiophen-3-yl-2-{3-[4-(2,2,2-trifluoro-ethyl)-phenyl]-thioureido}-propionic acid cyanomethyl-amide	G or N	*m/z*: 462.9 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-{3-[4-(2,2,2-trifluoro-ethyl)-phenyl]-thioureido}-propionic acid cyanoethyl-amide	G or N	*m/z*: 476.9 [M^+]

	**n = 1;** 3-Benzo[b]thiophen-3-yl-2-[3-(4-methoxy-phenyl)-thioureido]-propionic acid cyanomethyl-amide	G or N	*m/z*: 425.0 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-[3-(4-methoxy-phenyl)-thioureido]-propionic acid cyanoethyl-amide	G or N	*m/z*: 439.0 [M^+]
	**n = 1;** 3-Benzo[b]thiophen-3-yl-2-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-ylmethanesulfonylamino)-propionic acid cyanomethyl-amide	E or L	*m/z*: 474.2 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-ylmethanesulfonylamino)-propionic acid cyanoethyl-amide	E or L	*m/z*: 488.2 [M^+]
	**n = 1;** 3-Benzo[b]thiophen-3-yl-2-(thiophene-2-sulfonylamino)-propionic acid cyanomethyl-amide	E or L	*m/z*: 406.0 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-(thiophene-2-sulfonylamino)-propionic acid cyanoethyl-amide	E or L	*m/z*: 420.0 [M^+]
	**n = 1;** 3-Benzo[b]thiophen-3-yl-2-(4-trifluoromethoxy-benzenesulfonylamino)-propionic acid cyanomethyl-amide	E or L	*m/z*: 484.1 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-(4-trifluoromethoxy-benzenesulfonylamino)-propionic acid cyanoethyl-amide	E or L	*m/z*: 498.1 [M^+]
	n = 1; 3-Benzo[b]thiophen-3-yl-2-(4-*tert*-butyl-benzenesulfonylamino)-propionic acid cyanomethyl-amide	E or L	*m/z*: 456.2 [M^+]

	n = 2; 3-Benzo[b]thiophen-3-yl-2-(4-*tert*-butyl-benzenesulfonylamino)-propionic acid cyanoethyl-amide	E or L	*m/z*: 470.2 $[M^+]$
	n = 1; 3-Benzo[b]thiophen-3-yl-2-(4-chloro-benzenesulfonylamino)-propionic acid cyanomethyl-amide	E or L	*m/z*: 434.1 $[M^+]$
	n = 2; 3-Benzo[b]thiophen-3-yl-2-(4-chloro-benzenesulfonylamino)-propionic acid cyanoethyl-amide	E or L	*m/z*: 448.1 $[M^+]$
	n = 1; 3-Benzo[b]thiophen-3-yl-2-(4-methoxy-benzenesulfonylamino)-propionic acid cyanomethyl-amide	E or L	*m/z*: 430.1 $[M^+]$
	n = 2; 3-Benzo[b]thiophen-3-yl-2-(4-methoxy-benzenesulfonylamino)-propionic acid cyanoethyl-amide	E or L	*m/z*: 444.1 $[M^+]$
	n = 1; 3-Benzo[b]thiophen-3-yl-2-(quinoline-6-sulfonylamino)-propionic acid cyanomethyl-amide	E or L	*m/z*: 451.2 $[M^+]$
	n = 2; 3-Benzo[b]thiophen-3-yl-2-(quinoline-6-sulfonylamino)-propionic acid cyanoethyl-amide	E or L	*m/z*: 465.2 $[M^+]$
	n = 1; 3-Benzo[b]thiophen-3-yl-2-benzenesulfonylamino-propionic acid cyanomethyl-amide	E or L	*m/z*: 400.1 $[M^+]$
	n = 2; 3-Benzo[b]thiophen-3-yl-2-benzenesulfonylamino-propionic acid cyanoethyl-amide	E or L	*m/z*: 414.1 $[M^+]$
	n = 1; 1-Methyl-1H-indole-2-carboxylic acid [2-benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-amide	D or K	*m/z*: 417.1 $[M^+]$

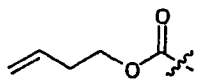
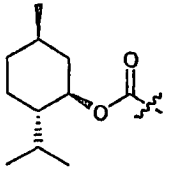
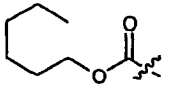
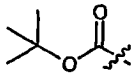
	n = 2; 1-Methyl-1H-indole-2-carboxylic acid [2-benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-amide	D or K	*m/z*: 431.0 $[M^+]$
	n = 1; 2-Propyl-pentanoic acid [2-benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-amide	D or K	*m/z*: 386.1 $[M^+]$
	n = 2; 2-Propyl-pentanoic acid [2-benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-amide	D or K	*m/z*: 400.0 $[M^+]$
	n = 1; 1-Methyl-cyclopropanecarboxylic acid [2-benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-amide	D or K	*m/z*: 342.0 $[M^+]$
	n = 2; 1-Methyl-cyclopropanecarboxylic acid [2-benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-amide	D or K	*m/z*: 356.0 $[M^+]$
	n = 1; Thiophene-2-carboxylic acid [2-benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-amide	D or K	*m/z*: 369.9 $[M^+]$
	n = 2; Thiophene-2-carboxylic acid [2-benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-amide	D or K	*m/z*: 383.9 $[M^+]$
	n = 1; *N*-[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-3-trifluoromethyl-benzamide	D or K	*m/z*: 431.9 $[M^+]$
	n = 2; *N*-[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-3-trifluoromethyl-benzamide	D or K	*m/z*: 445.9 $[M^+]$
	n = 1; Biphenyl-2-carboxylic acid [2-benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-amide	D or K	*m/z*: 440.0 $[M^+]$

	**n = 2;** Biphenyl-2-carboxylic acid [2-benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-amide	D or K	*m/z*: 454.0 [M^+]
	**n = 1;** 4-Acetylamino-*N*-[2-benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-benzamide	D or K	*m/z*: 421.0 [M^+]
	n = 2; 4-Acetylamino-*N*-[2-benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-benzamide	D or K	*m/z*: 435.0 [M^+]
	**n = 1;** 3-Benzo[b]thiophen-3-yl-2-(2-1*H*-indol-3-yl-acetylamino)-propionic acid cyanomethyl-amide	D or K	*m/z*: 417.1 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-(2-1*H*-indol-3-yl-acetylamino)-propionic acid cyanoethyl-amide	D or K	*m/z*: 431.0 [M^+]
	**n = 1;** 3-Benzo[b]thiophen-3-yl-2-(3-1*H*-indol-3-yl-propionylamino)-propionic acid cyanomethyl-amide	D or K	*m/z*: 431.0 [M^+]
	n = 2; 3-Benzo[b]thiophen-3-yl-2-(3-1*H*-indol-3-yl-propionylamino)-propionic acid cyanoethyl-amide	D or K	*m/z*: 445.0 [M^+]
	**n = 1;** *N*-[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-4-(1*H*-indol-3-yl)-butyramide	D or K	*m/z*: 445.0 [M^+]
	n = 2; *N*-[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-4-(1*H*-indol-3-yl)-butyramide	D or K	*m/z*: 459.0 [M^+]

	**n = 1**; *N*-[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-benzamide	D or K	*m/z*: 364.0 [M^+]
	n = 2; *N*-[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-benzamide	D or K	*m/z*: 378.0 [M^+]
	**n = 1**; 3-Chloromethyl-*N*-[2-benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-benzamide	D or K	*m/z*: 412.0 [M^+]
	n = 2; 3-Chloromethyl-*N*-[2-benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-benzamide	D or K	*m/z*: 426.0 [M^+]
	**n = 1**; 4-Chloromethyl-*N*-[2-benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-benzamide	D or K	*m/z*: 411.9 [M^+]
	n = 2; 4-Chloromethyl-*N*-[2-benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-benzamide	D or K	*m/z*: 426.0 [M^+]
	**n = 1**; *N*-[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-2-fluoro-benzamide	D or K	*m/z*: 381.9 [M^+]
	n = 2; *N*-[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-2-fluoro-benzamide	D or K	*m/z*: 395.9 [M^+]
	**n = 1**; *N*-[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-2-nitro-benzamide	D or K	*m/z*: 408.9 [M^+]
	n = 2; *N*-[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-2-nitro-benzamide	D or K	*m/z*: 422.9 [M^+]

	n = 1; *N*-[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-acrylamide	D or K	*m/z*: 313.9 $[M^+]$
	n = 2; *N*-[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-acrylamide	D or K	*m/z*: 327.9 $[M^+]$
	n = 1; 3-Benzo[b]thiophen-3-yl-2,2-dimethyl-propionic acid cyanomethyl-amide	D or K	*m/z*: 344.0 $[M^+]$
	n = 2; 3-Benzo[b]thiophen-3-yl-2,2-dimethyl-propionic acid cyanoethyl-amide	D or K	*m/z*: 358.0 $[M^+]$
	n = 1; 3-Benzo[b]thiophen-3-yl-2-(2-methoxy-acetylamino)-propionic acid cyanomethyl-amide	D or K	*m/z*: 332.0 $[M^+]$
	n = 2; 3-Benzo[b]thiophen-3-yl-2-(2-methoxy-acetylamino)-propionic acid cyanoethyl-amide	D or K	*m/z*: 346.0 $[M^+]$
	n = 1; *N*-[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-oxalamic acid methyl ester		*m/z*: 346.0 $[M^+]$
	n = 2; *N*-[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-oxalamic acid methyl ester		*m/z*: 360.0 $[M^+]$
	n = 1; *N*-[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-phthalamic acid	B or I	*m/z*: 407.9 $[M^+]$
	n = 2; *N*-[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-phthalamic acid	B or I	*m/z*: 421.9 $[M^+]$

	n = 1; *N*-[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-succinamic acid	B or I	*m/z*: 359.9 $[M^+]$
	n = 2; *N*-[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-succinamic acid	B or I	*m/z*: 373.9 $[M^+]$
	n = 1; 3-[2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethylcarbamoyl]-acrylic acid	B or I	*m/z*: 358.0 $[M^+]$
	n = 2; 3-[2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethylcarbamoyl]-acrylic acid	B or I	*m/z*: 372.0 $[M^+]$
	n = 1; [2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-carbamic acid isobutyl ester	C or J	*m/z*: 360.0 $[M^+]$
	n = 2; [2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-carbamic acid isobutyl ester	C or J	*m/z*: 374.0 $[M^+]$
	n = 1; [2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-carbamic acid butyl ester	C or J	*m/z*: 360.0 $[M^+]$
	n = 1; [2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-carbamic acid butyl ester	C or J	*m/z*: 374.0 $[M^+]$
	n = 1; [2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-carbamic acid cyanomethyl ester	C or J	*m/z*: 341.9 $[M^+]$
	n = 2; [2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-carbamic acid cyanomethyl ester	C or J	*m/z*: 355.9 $[M^+]$

	n = 1; [2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-carbamic acid but-3-enyl ester	C or J	*m/z*: 358.0 [M^+]
	n = 2; [2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-carbamic acid but-3-enyl ester	C or J	*m/z*: 372.0 [M^+]
	n = 1; [2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-carbamic acid 2-isopropyl-5-methyl-cyclohexyl ester	C or J	*m/z*: 442.0 [M^+]
	n = 2; [2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-carbamic acid 2-isopropyl-5-methyl-cyclohexyl ester	C or J	*m/z*: 456.0 [M^+]
	n = 1; [2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-carbamic acid hexyl ester	C or J	*m/z*: 388.0 [M^+]
	n = 2; [2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-carbamic acid hexyl ester	C or J	*m/z*: 402.0 [M^+]
	n = 1; [2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-carbamic acid tert-butyl ester δ = 1.28 (s, 9 H), 3.05 (dd, 1 H, J = 9.9, J = 14.2 Hz), 3.22 (dd, 1 H, J = 4.6, J = 14.2 Hz), 4.15 (m, 2 H), 4.32 (m, 1 H), 7.15 (d, 1 H, J = 8.4 Hz), 7.35-7.48 (m, 3 H), 7.89-7.98 (m, 2 H), 8.74 (m, 1 H).		*m/z*: 359.9 [M^+]

	n = 2; [2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-carbamic acid tert-butyl ester δ = 1.29 (s, 9 H), 2.61 (m, 2 H), 3.04 (m, 2 H), 3.22 (m, 2 H), 3.27-3.40 (m, 4 H), 4.28 (m, 1 H), 7.01 (d, 1 H, J = 8.2 Hz), 7.40 (m, 2 H), 7.90 (d, 1 H, J = 7.3 Hz), 7.96 (d, 1 H, J = 7.9 Hz), 8.38 (m, 1 H).		*m/z*: 373.8 [M^+]
	n = 1; [2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-carbamic acid methyl ester	C or J	*m/z*: 318.0 [M^+]
	n = 2; [2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-carbamic acid methyl ester	C or J	*m/z*: 332.0 [M^+]
	n = 1; [2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-carbamic acid ethyl ester	C or J	*m/z*: 332.0 [M^+]
	n = 2; [2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-carbamic acid ethyl ester	C or J	*m/z*: 346.0 [M^+]
	n = 1; [2-Benzo[b]thiophen-3-yl-1-(cyanomethyl-carbamoyl)-ethyl]-carbamic acid 9*H*-fluoren-9-ylmethyl ester	C or J	*m/z*: 481.9 [M^+]
	n = 2; [2-Benzo[b]thiophen-3-yl-1-(cyanoethyl-carbamoyl)-ethyl]-carbamic acid 9*H*-fluoren-9-ylmethylester	C or J	*m/z*: 495.9 [M^+]

EXAMPLE 12

Specificity of inhibition of certain enzymes by compounds according to the present invention

In order to characterize the specificity of various compounds the following assays were performed. PPIase activity of hPin1, hCyp18, LpCyp18, hFKBP12 and EcParvulin was measured using the protease-coupled PPIase assay according to Fischer et al. (Fischer, G.; Bang, H.; Mech, C. Determination of enzymatic catalysis fort he cis-trans-isomerization of peptide binding in proline-containing peptides. [German] Biomed. Biochem. Acta 1984, 43, 1101-1111; Hennig et al., Selective Inactivation of Parvulin-like peptidyl-prolyl cis/trans isomerases by Juglon, Biochemistry. 1998, 37(17):5953-5960). For hPin1 measurements Ac-Ala-Ala-Ser(PO_3H_2) -Pro-Arg-pNA was used as a substrate and trypsin (final concentration 190 µg/ml) as an isomer-specific protease. Activity measurements of other PPIases were made with the substrate peptide Suc-Ala-Phe-Pro-Phe-pNA and the protease α-chymotrypsin (final concentration 470 µg/ml). The assays were performed in a final reaction volume of 150 µL at final concentrations of 6 nM hPin1, 10 nM hCyp18, 5 nM LpCyp18, 20 nM EcParvulin and 20 nM hFKBP12, respectively, and 120 µM substrate peptide in 35 mM HEPES (pH 7.8). For inhibition experiments 100-0.01 µM of effector freshly diluted from a DMSO stock solution were added. The amount of solvent was kept constant within each experiment, usually below 0.3% (v/v). All reactions were started by addition of protease. The test was performed by observing the released 4-nitroaniline at 390 nm with a MR5000 UV/Vis spectrophotometer (Dynex) at 6°C. Data were evaluated by calculation of pseudo-first-order rate constants k_{obs} in presence of PPIase and PPIase/effector, respectively, and corrected for the contribution of the non-catalyzed reaction (k_0). Inhibition constants IC_{50} were calculated using SigmaPlot 8.0 (SPSS).

The following target enzymes which are all rotamases belonging to different families of rotamases were used:

T-1: Protein interacting with NIMA (-kinase), hPin1

T-2: First described human Rapamycin receptor, hFKBP12

T-3: Human Cyclosporin A receptor with 18 kDa molecular weight, hCyp18

T-4: Leishmonia pneumophila virulence Cyclosporin A receptor with 18 kDa molecular weight, LpCyp18

T-5: Bacterial Juglon sensitive non proteolytic enzyme, EcParv

These rotamases are known in the art. Their production and characteristics may be taken from the following references.

Review about all PPIase families

Gothel, S. F.; Marahiel, M. A. TI Peptidyl-prolyl cis-trans isomerases, a superfamily of ubiquitous folding catalysts [Review]. Cell. Molec. Life Sci. 1999, 55, 423-436

Pin1

Lu, K. P.; Hanes, S. D.; Hunter, T. (1996) A human peptidyl-prolyl isomerase essential for regulation of mitosis. *Nature* **1996**, *380*, 544-547.

Yaffe, M. B.; Schutkowski, M.; Shen, M. H.; Zhou, X. Z.; Stukenberg, P. T.; Rahfeld, J. U.; Xu, J.; Kuang, J.; Kirschner, M. W.; Fischer, G.; Cantley, L. C.; Lu K. P. Sequence-specific and phosphorylation-dependent praline isomerization – A potential mitotic regulatory mechanism. *Science* **1997**, *278*, 1957-1960.

Shen, M.; Stukenberg, P. T.; Kirschner, M. W.; Lu, K. P. The essential mitotic peptidyl-prolyl isomerase Pin1 binds and regulates mitosis-specific phosphoproteins. *Genes Developm.* **1998**, *12*, 706-720.

EcParvulin

Rahfeld JU. Schierhorn A. Mann K. Fischer G. A novel peptidyl-prolyl cis/trans isomerase from Escherichia coli. *FEBS Letters.* **1994**, *343*, 65-69

Rahfeld JU. Rucknagel KP. Schelbert B. Ludwig B. Hacker J. Mann K. Fischer G. Confirmation of the existence of a third family among peptidyl-prolyl cis/trans isomerases. Amino acid sequence and recombinant production of parvulin. *FEBS Letters.* **1994**, *352*, 180-184

FKBPs (including FKBP12) and Cyclophilins (including Cyp18)

For recent reviews on cyclophilins and FKBPs and their effectors, see: (a) Fischer, G. Peptidyl-prolyl *cis/trans* isomerases and their effectors. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1415-1436. (b) Galat, A.; Metcalfe, S. M. Peptidylproline *cis/trans* isomerases. *Prog. Biophys. Molec. Biol.* **1995**, *63*, 67-118.

LpCyp18

Schmidt B. Tradler T. Rahfeld JU. Ludwig B. Jain B. Mann K. Rucknagel KP. Janowski B. Schierhorn A. Kullertz G. Hacker J. Fischer G. A cyclophilin-like peptidyl-prolyl cis/trans isomerase from Legionella pneumophila--characterization, molecular cloning and overexpression. *Mol. Microbiol.* **1996**, *21*,1147-1160

In order to cluster the various rotamase inhibitors the following classes were defined with "A" indicating the most potent rotamase inhibitor.

A: $IC_{50} < 5\ \mu M$

B: $5\ \mu M < IC_{50} < 10\ \mu M$

C: $10\ \mu M < IC_{50} < 50\ \mu M$

D: $50\ \mu M < IC_{50} < 100\ \mu M$

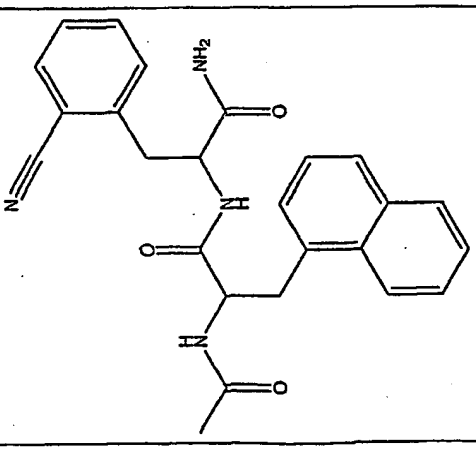
E: $IC_{50} > 100\ \mu M$

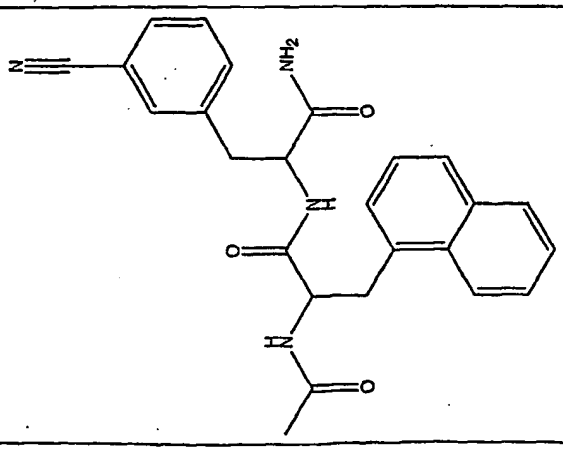
Table

Specificity of the inhibition with rotamases

Compound	N°	Target				
		T-1	T-2	T-3	T-4	T-5
	1	A	E	E	E	E
	2	B	E	E	E	D
	3	B	E	E	E	E

Compound	N°	Target				
		T-1	T-2	T-3	T-4	T-5
	4	A	E	E	E	C
	5	A	E	E	E	
	6	B	E	E	E	
	7	B	E	E	E	C

Compound	N°	Target					
		T-1	T-2	T-3	T-4	T-5
	8	A	E	E	E	B

Compound	N°	Target				
		T-1	T-2	T-3	T-4	T-5
	9	B	E	E	E	B

As may be taken from the above table the following compounds 1, 5, 8, are of class A and are thus extremely specific for hPin1.

The features of the present invention disclosed in the specification, the claims and/or the drawings may both separately and in any combination thereof be material for realizing the invention in various forms thereof.